Risk of pediatric asthma morbidity from multipollutant exposures.

Principal Investigator:
Ralph J. Delfino, MD, PhD

Co-investigators:
Michael J. Kleeman, PhD
Jun Wu, PhD
Daniel J. Gillen, PhD
Bruce Nickerson, MD

Outline

- Background
  - Epidemiologic research of acute asthma and air pollution
  - Data gaps / Exposure assessment
- Overview of Study
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Definition of Asthma

- A chronic inflammatory disorder of the airways.

- Many cells and cellular elements play a role in airway inflammation.

- Chronic inflammation is associated with airway (bronchial) hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing

- Widespread, variable, and often reversible airflow limitation.

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Acute asthma outcomes linked to air pollution in experimental and/or epidemiologic studies

- Increased bronchial hyperresponsiveness;

- Decreased lung function;

- Increased airway inflammation and oxidative stress;

- Increased asthma symptoms & prn medication use;

- Increased asthma morbidity from respiratory infections;

- Hospital admissions and ED visits (**time series studies** – largely reliant on **ambient data**).

Panel Studies, Key Findings

- Exposure markers of traffic-related air pollutants (**TRAP**) such as NO_x and elemental carbon (EC) are associated with:
  - Asthma symptoms;
  - Decreased expiratory lung function (FEV_1); and
  - Increased airway inflammation:
    represented by daily fractional exhaled NO (FeNO).

- Associations with ambient PM mass are either not observed or are confounded by TRAP markers such as EC.

- Personal exposure measurements are significantly associated with asthma outcomes more often than ambient exposures.

Important Time Series Studies, Key Findings

- 69,375 asthma hospital admissions in New York City
  Silverman and Ito. J Allergy Clin Immunol 2010;125:367-73
  90,000 ED visits for pediatric asthma in Atlanta
  Strickland et al. Am J Respir Crit Care Med. 2010;182:307-16
  400,000 asthma ED visits to 14 hospitals in Canada
  Stieb et al. Environmental Health 2009;8:25

- Asthma morbidity is associated with ozone, $PM_{2.5}$, and primary combustion aerosols and gases (indicators of TRAP) especially in the warm season.

- Associations of asthma morbidity with ozone has been to some extent independent of associations with $PM_{2.5}$ and with TRAP.

Age-related association of 69,375 asthma hospital admissions with co-regressed $PM_{2.5}$ and O_3 in New York City, warm seasons
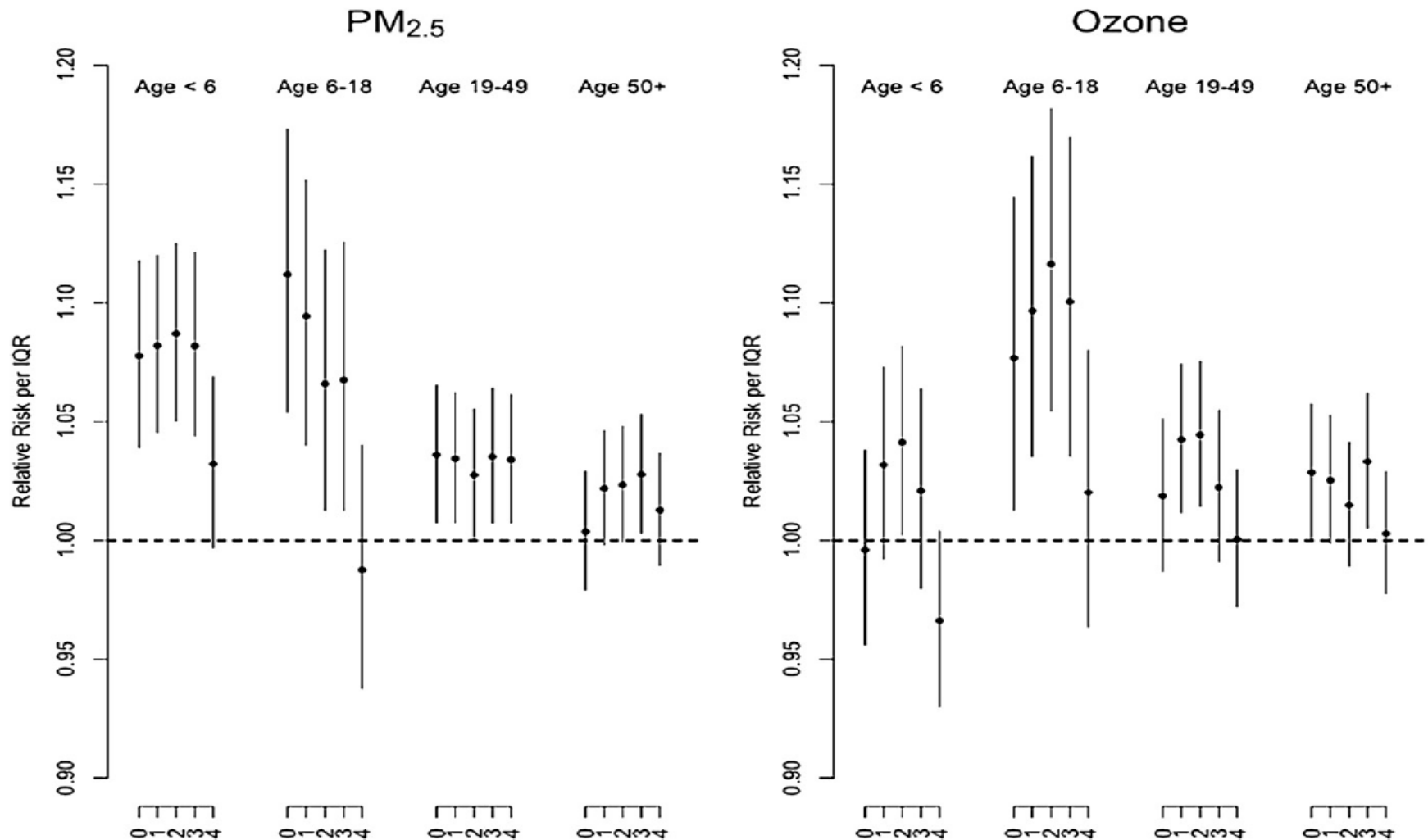
Silverman and Ito. J Allergy Clin Immunol 2010;125:367-73

FIG 4. Estimated relative risks of asthma hospitalization per IQR of $PM_{2.5}$ and ozone for individual lags 0 through 4 in a 2-pollutant model (evaluated at the same lag day for both pollutants) by age group in years, adjusting for temporal trends, day of the week, and immediate and delayed weather effects.

Questions emerging from time series analyses of asthma hospital admissions and ED Visits

- What contributes to independent effects of O_3 and $PM_{2.5}$?
  Secondary organic aerosol fractions of $PM_{2.5}$ and/or primary (traffic-related) fractions of $PM_{2.5}$ not well correlated with O_3?

- Given the high spatial variability TRAP, what is the effect of local variation in TRAP on associations between asthma and ambient air pollution?

Background: SES

- Observed adverse effects of poverty on asthma severity may be from decreased access to health care, correlated risk factors such as exposure to passive smoke or indoor allergens, and psychosocial stressors.

- Children in low income communities also may be more likely to live near high density traffic.

- SES could result in potential confounding of associations between asthma outcomes and air pollution.

- However, studies suggest that poverty increases asthma susceptibility to the effects of both TRAP and ambient O_3:

  Meng et al. 2008 Ann Epidemiol. 18:343-50;
  O'Neill et al. 2003 Environ Health Perspect. 111:1861-70;
  Lin S et al. 2008 Environ Health Perspect 116:1725-30.

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Background: Data Gaps

- Limited knowledge about the effects on asthma morbidity by different **particle size fractions** (especially ultrafine particles), their **sources** and <u>components</u>.

- Lack of data on differences in associations of asthma morbidity with exposures to **local versus regional** (ambient) air pollutants.

- Little is know regarding differences in health effects in human populations by two important classes of $PM_{2.5}$ constituents:

    - 1) **Primary organic aerosols (POA)** from combustion sources, especially traffic-related sources in LA basin;

    - 2) **Secondary organic aerosols (SOA),** which are photochemically-produced from combustion-related, industrial, and biogenic volatile or semi-volatile precursors.

Limitations of Ambient Exposure Data for Asthma and Air Pollution Research

- Epidemiologic studies have largely used and shown associations between asthma outcomes and ambient "principal criteria air pollutants" regulated by EPA and measured at widely dispersed locations: PM_{10}, $PM_{2.5}$, O_3, NO_2, CO, SO_2

- To what extent has exposure error affected results?

- What are the effects of unmeasured exposure to toxic air pollutants (e.g., combustion-related and photochemically-related organic chemicals) from sources <u>near</u> the subject?
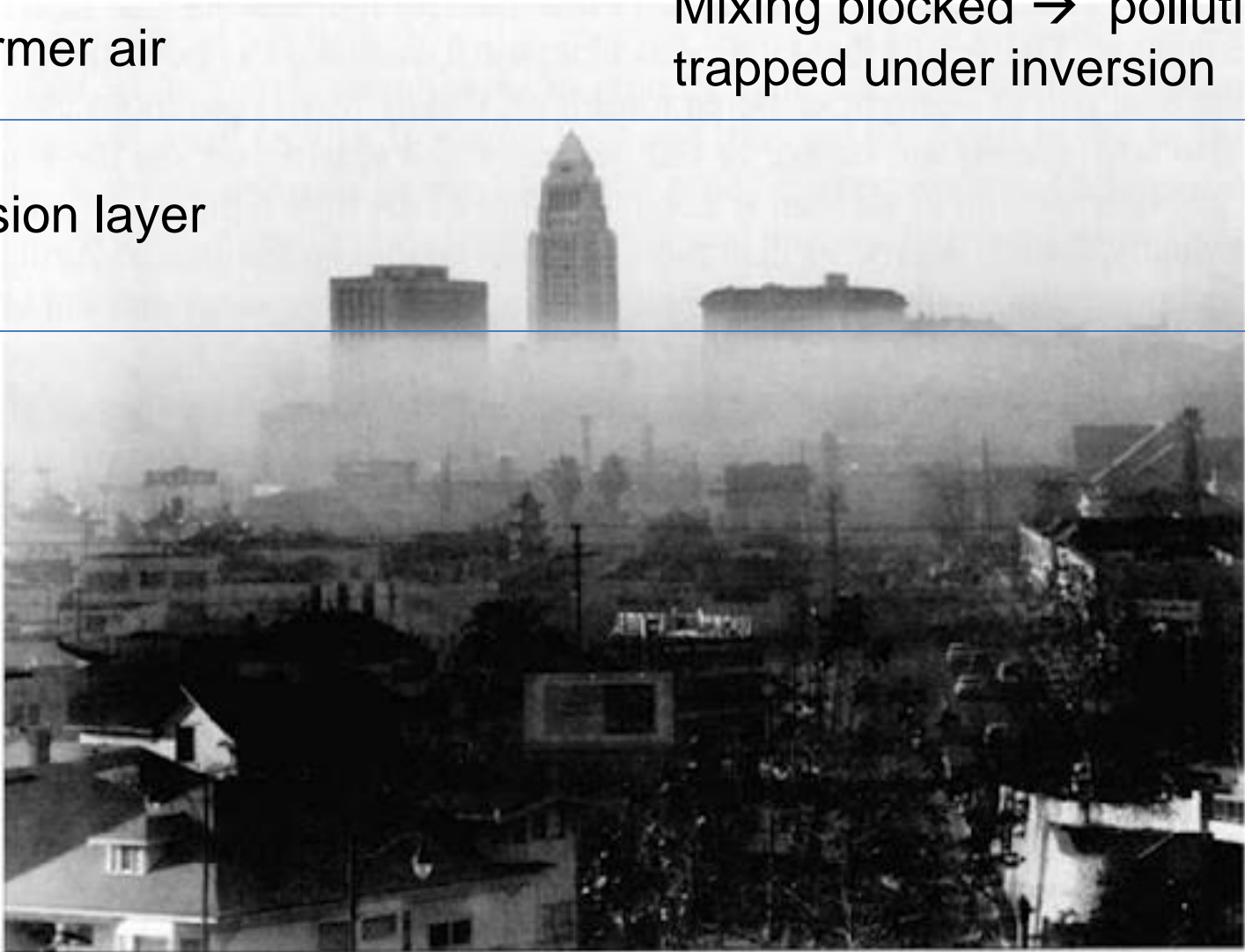
Spatial Variability in Traffic-related Air Pollution

Zhu et al. *J Air Waste Manage Assoc* 2002;52:1032-1042.
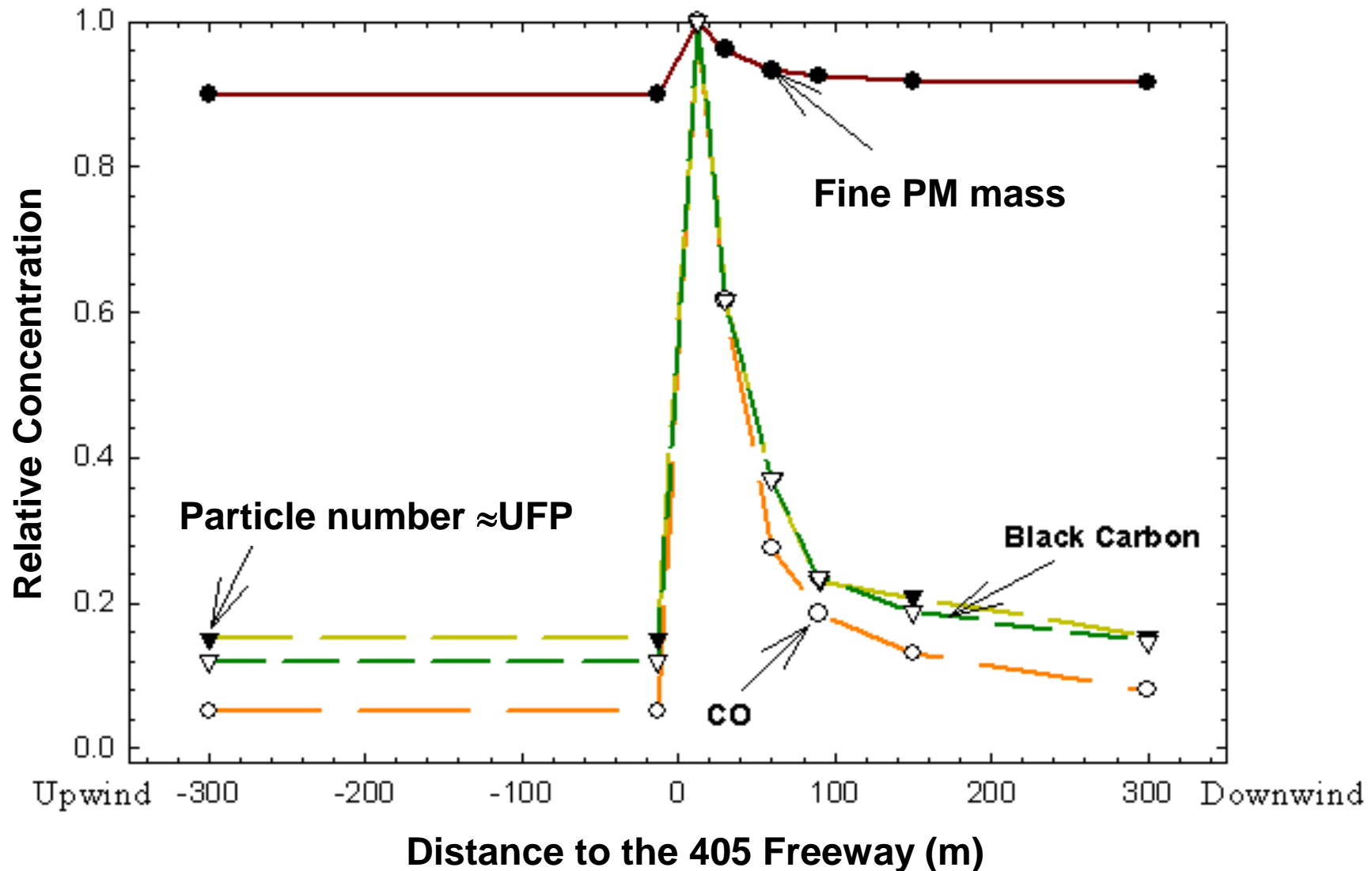
Temporal-spatial variability in Traffic-related Air Pollution

Air inversion layer with cold stagnant air

Warmer air

Mixing blocked → pollution trapped under inversion

Inversion layer

Overview of Study

- **Task 1. To estimate exposures for children with asthma to primary and secondary organic aerosols.** UC Davis /California Institute of Technology (UCD/CIT) Source Oriented Chemical Transport Model– POA, SOA, size-resolved mass and POA source apportionment (coinvestigator Mike Kleeman) .

- **Task 2. To assess the risk of emergency department visits and hospital admissions for asthma in children from exposure to both traffic-related particles near their homes and local ambient primary and secondary organic aerosols and O$_3$.** UCD/CIT model data , TRAP near geocoded subject residences, and ambient air pollution.

Overview of Study

- **Task 3. To stratify subjects based on recurrence of hospital encounters in order to assess whether children with multiple encounters show the strongest associations with air pollutants.**

- **Task 4. To assess effect modification of associations by subject demographic and socioeconomic characteristics.** Included neighborhood SES, health insurance, race-ethnicity, sex, and age group
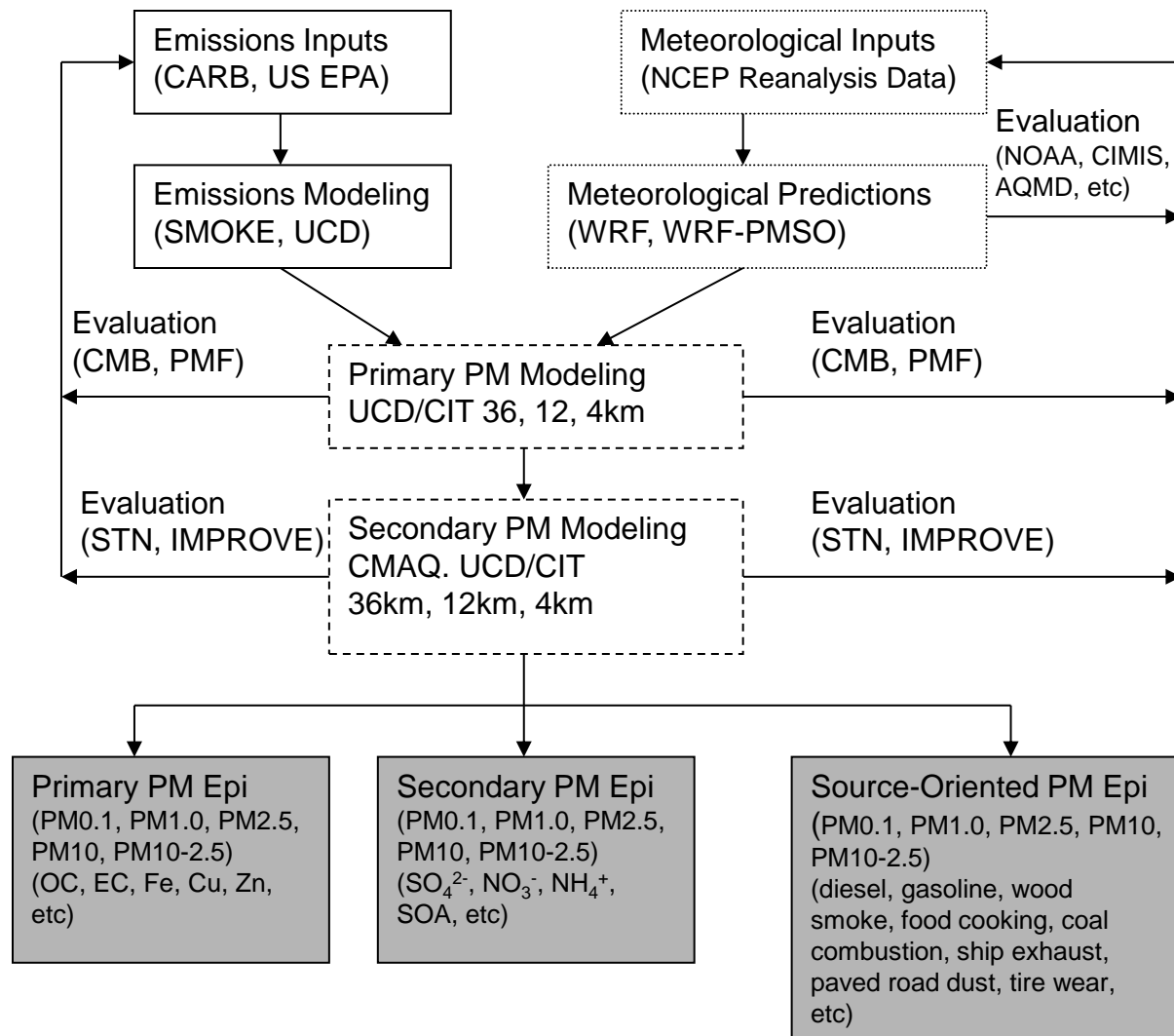
Task 1

- To estimate exposures for children with asthma to primary and secondary organic aerosols.
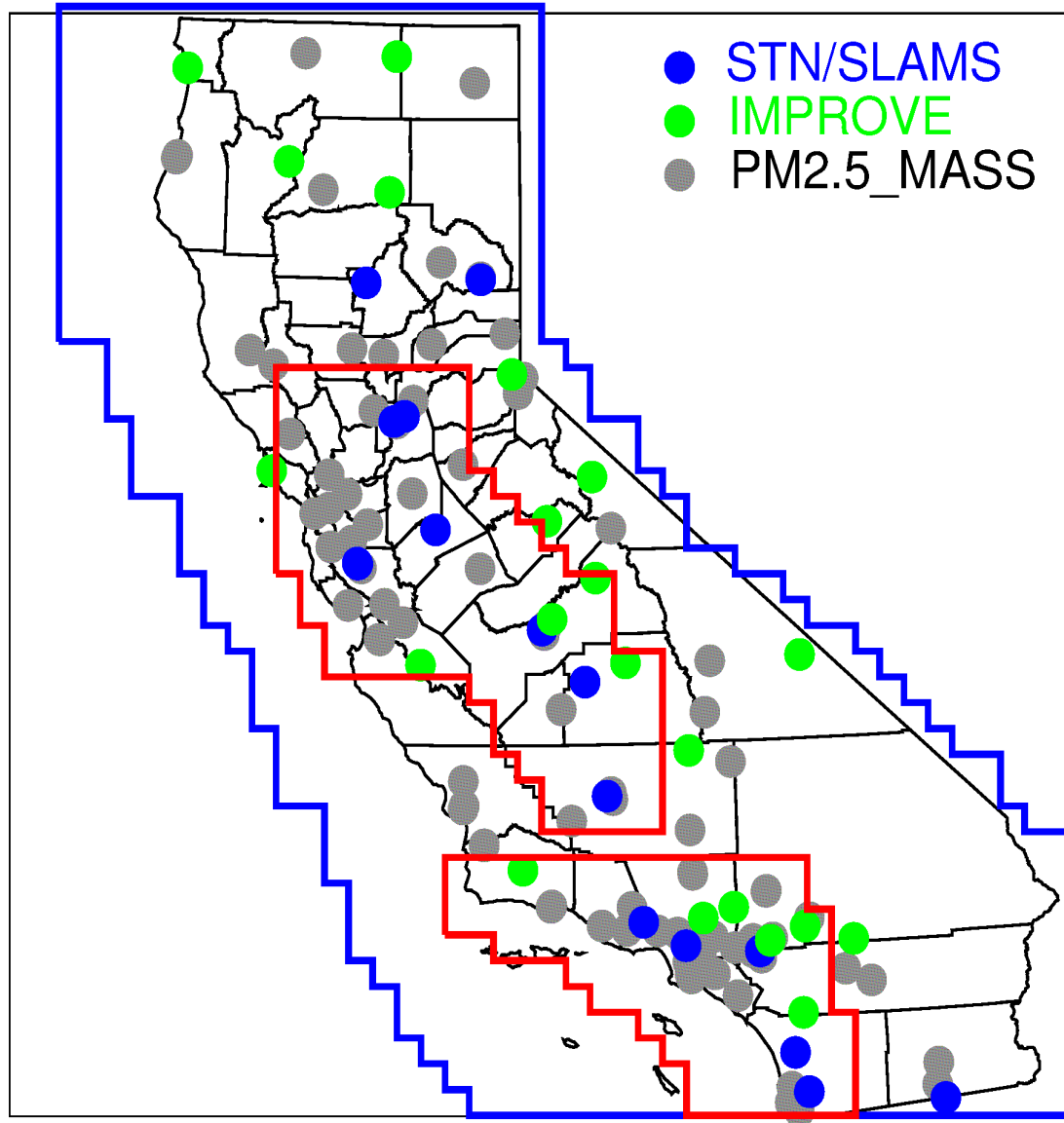
Michael Kleeman

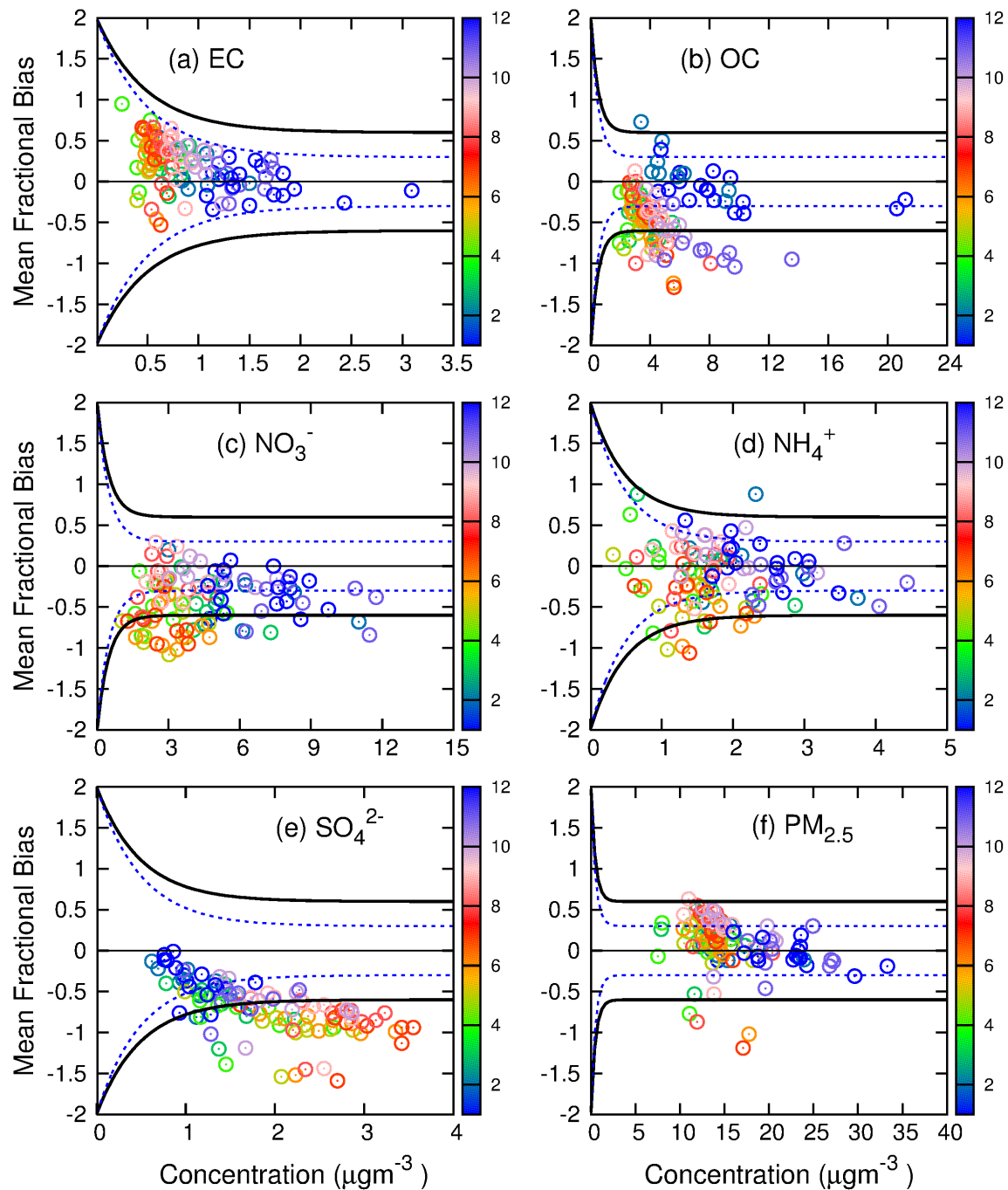Department of Civil and Environmental Engineering,
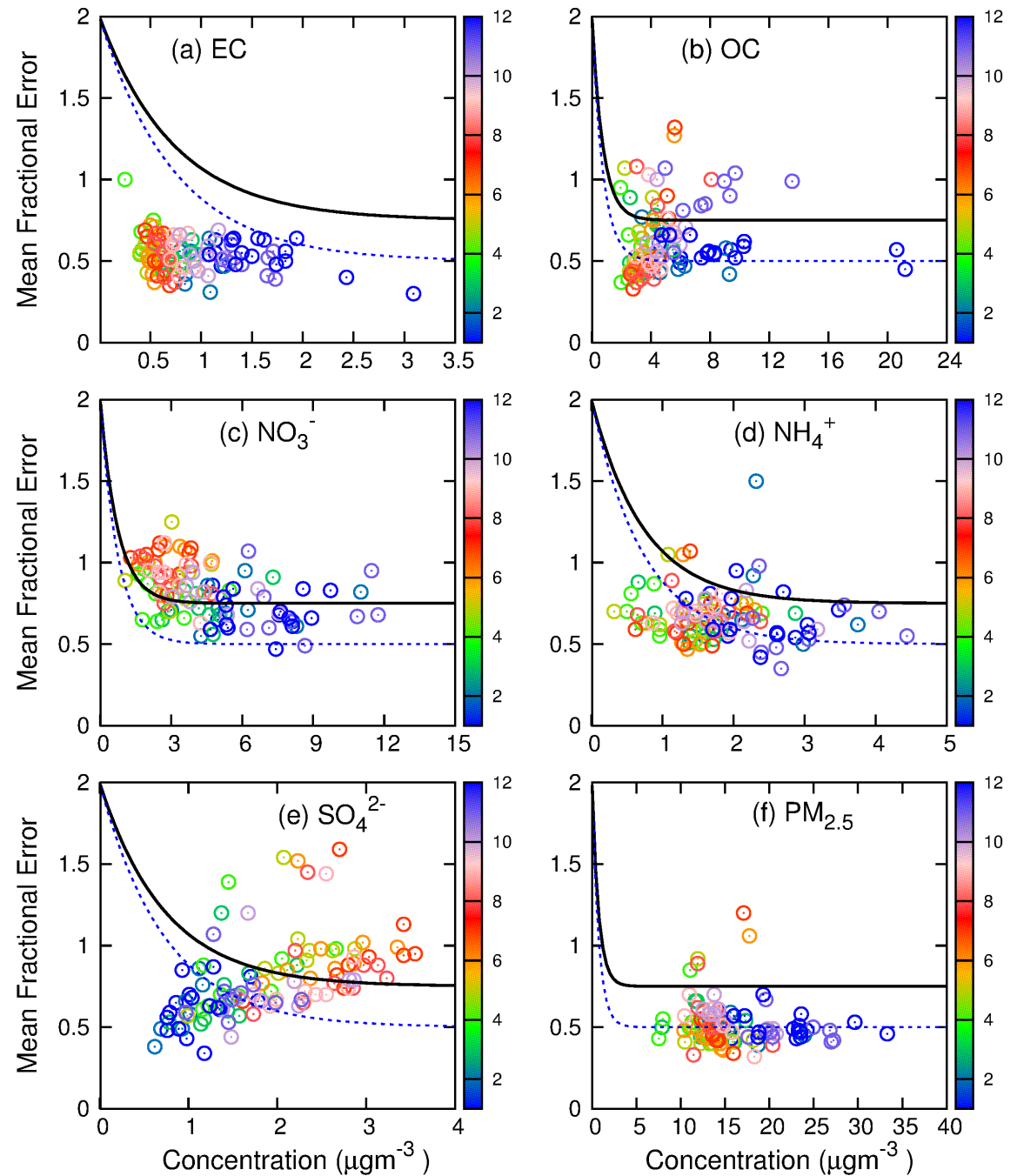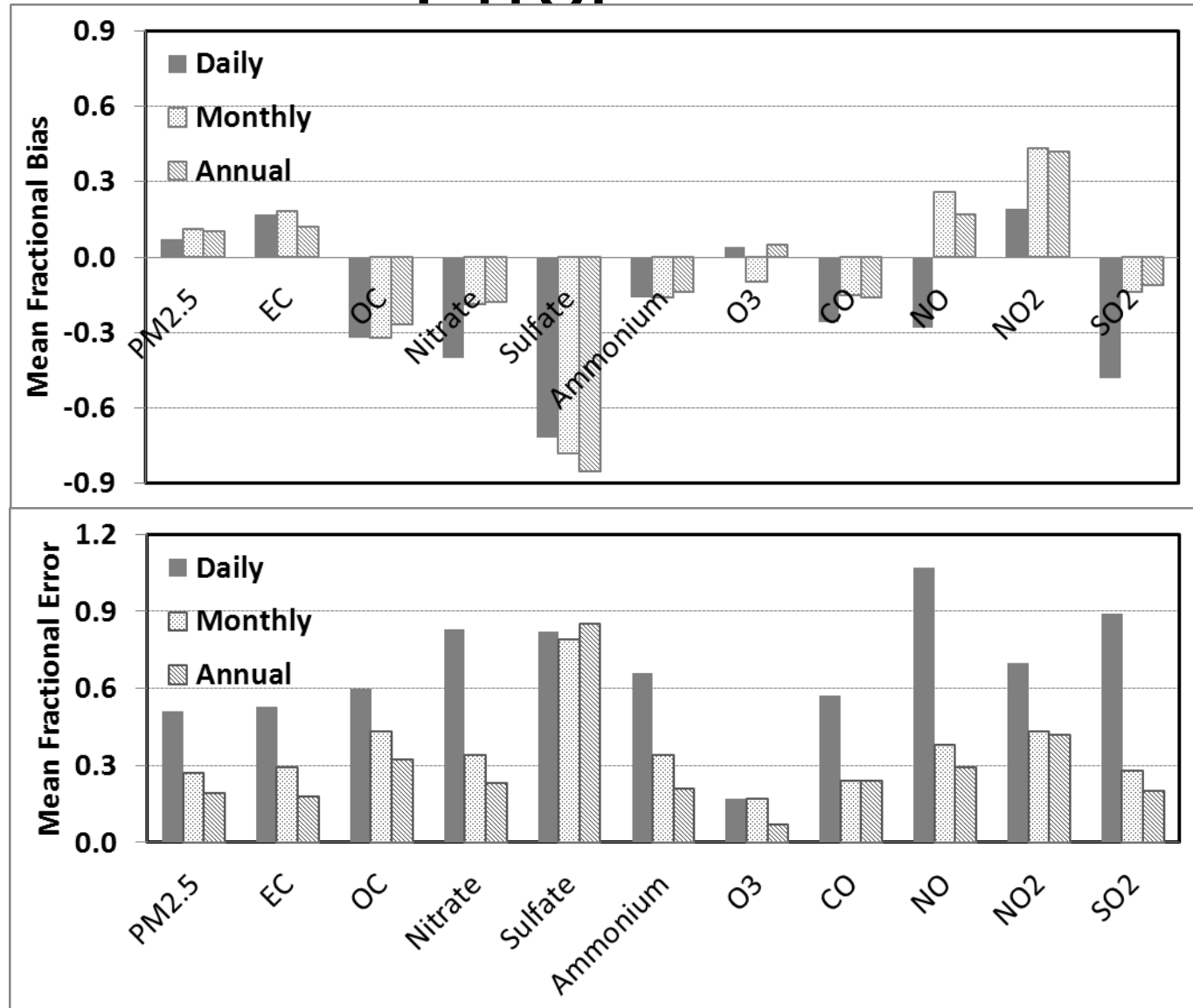UC Davis

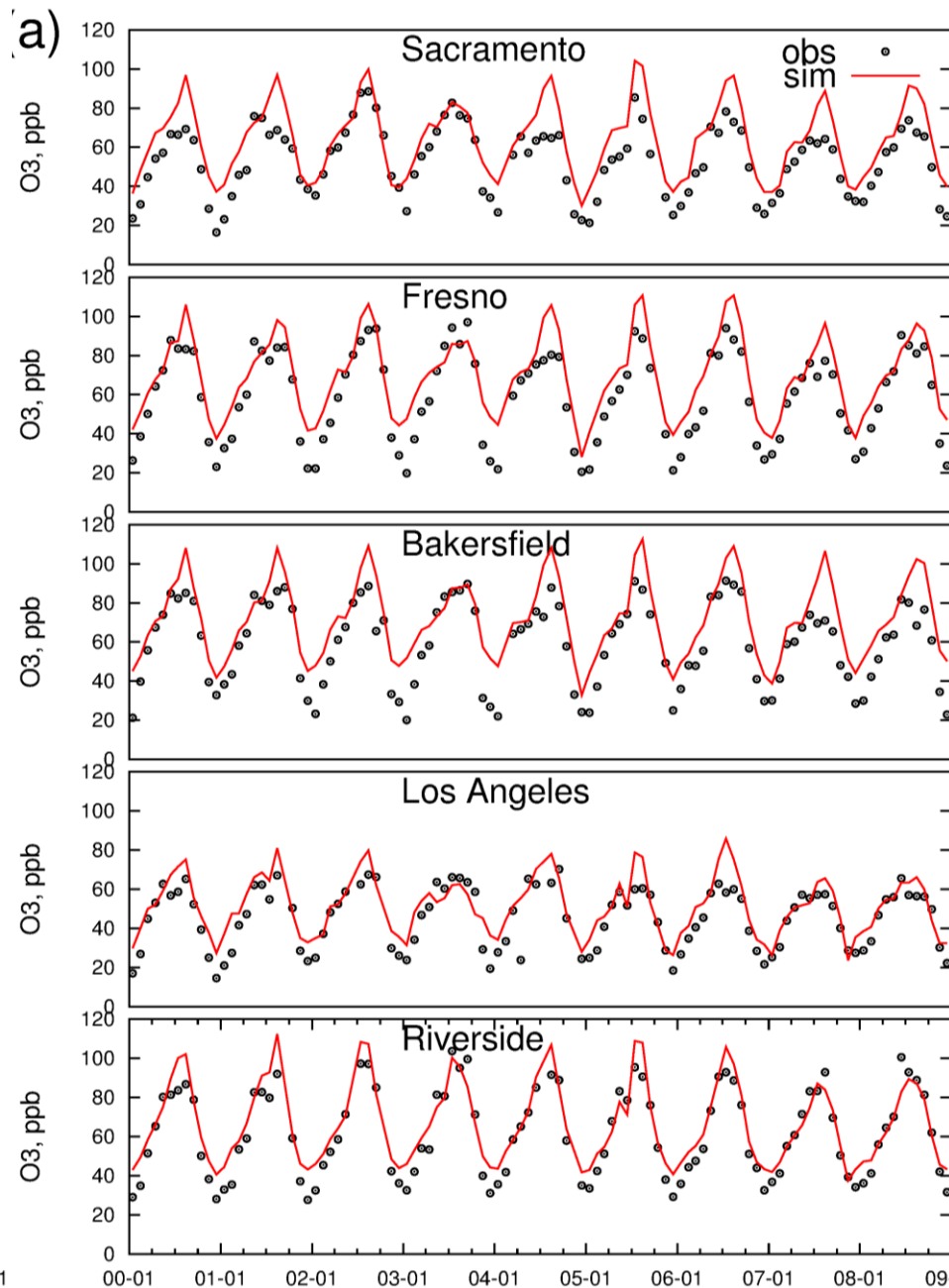# Exposure Modeling Framework

Spatial Domains and Resolution

Monthly Mean Fractional Bias

Monthly Mean Fractional Error

Influence of Averaging Time on Error

c)

Sacramento — obs, sim

Fresno

Bakersfield

Los Angeles

Riverside

a)

Sacramento — obs, sim

Fresno

Bakersfield

Los Angeles

Riverside

(g) Time series of observed (obs) and simulated (sim) EC ($\mu g/m^3$) and (e) N(V) ($\mu g/m^3$) at Sacramento, Fresno, Bakersfield, Los Angeles, and Riverside.
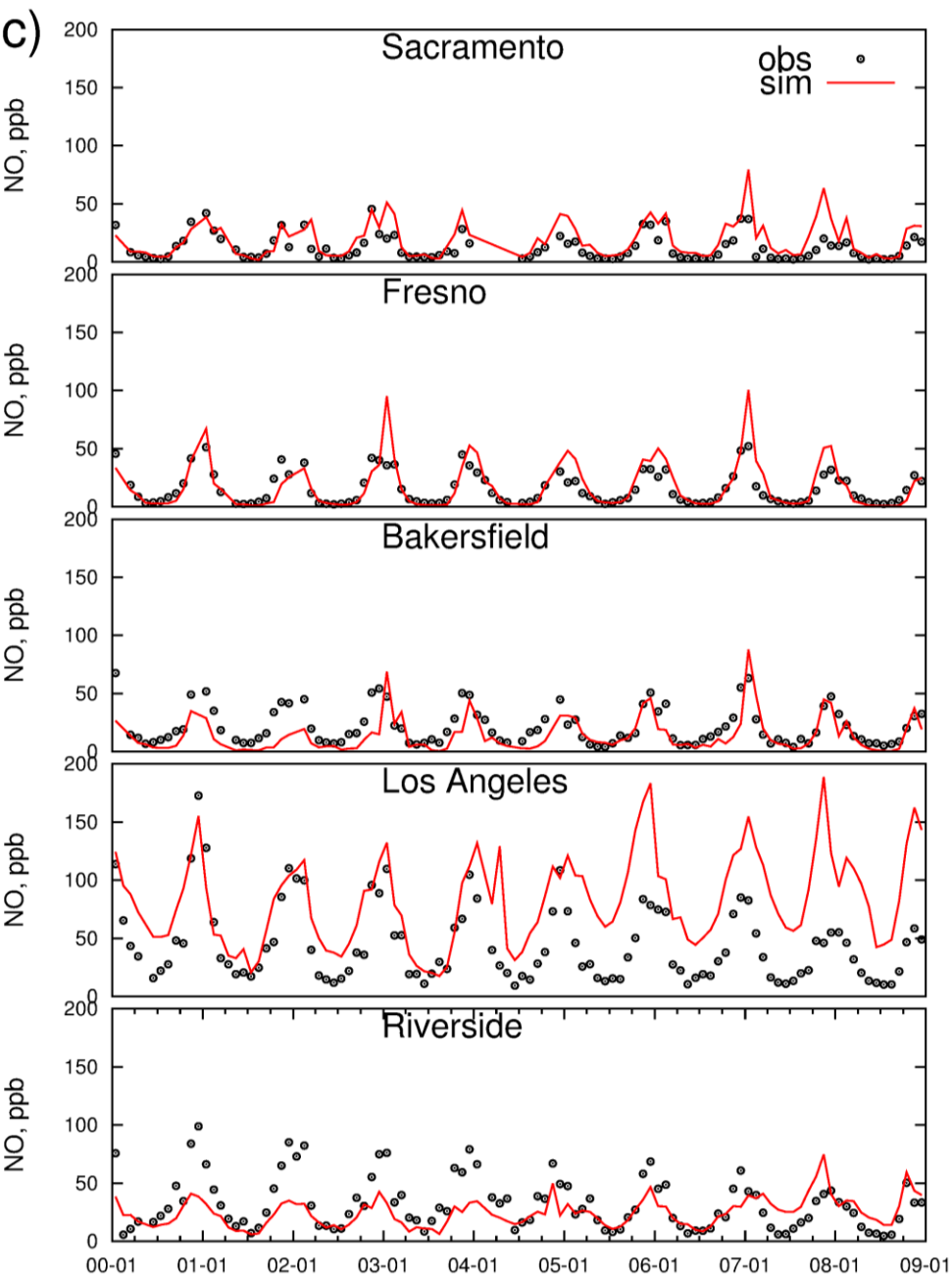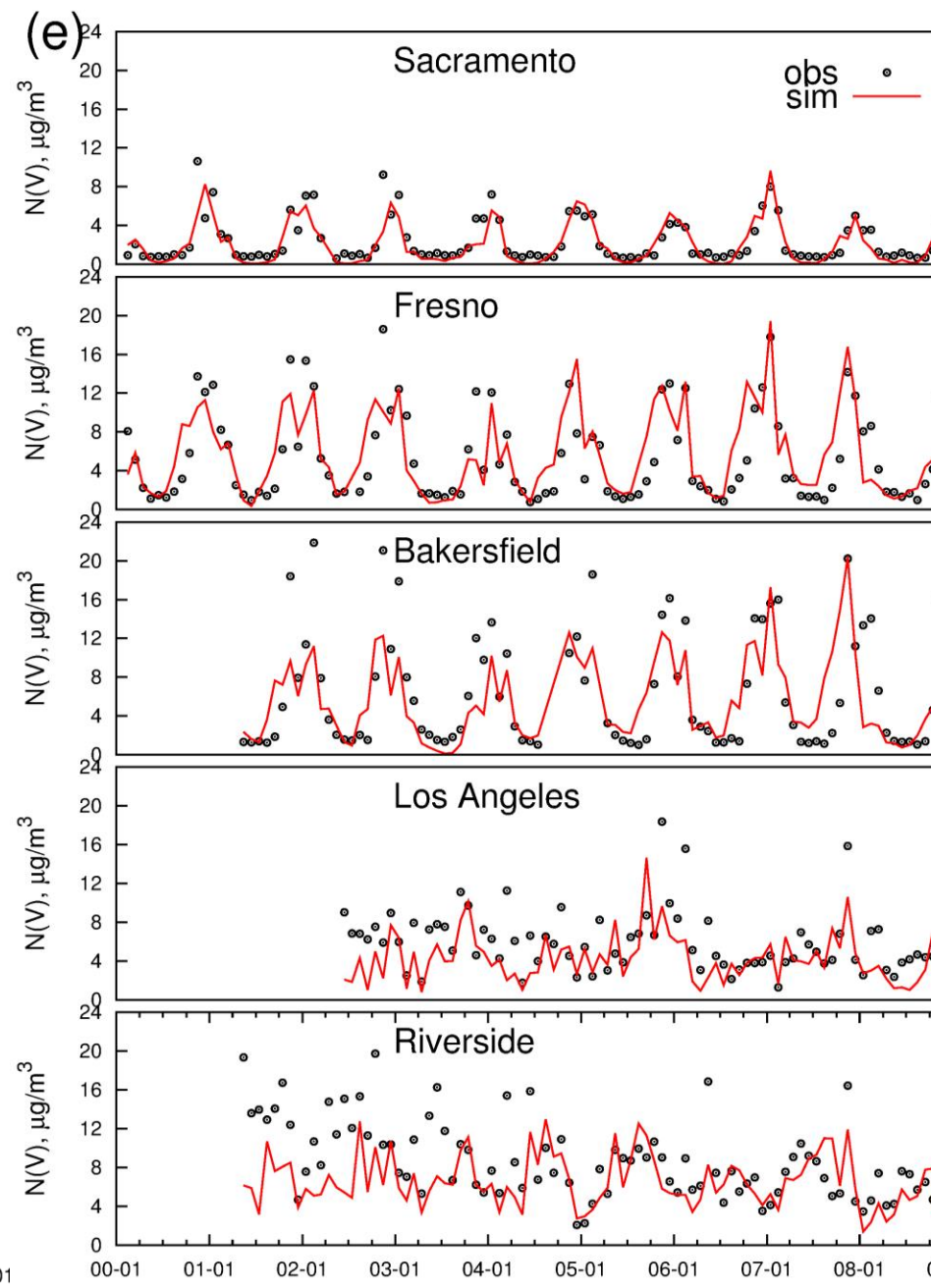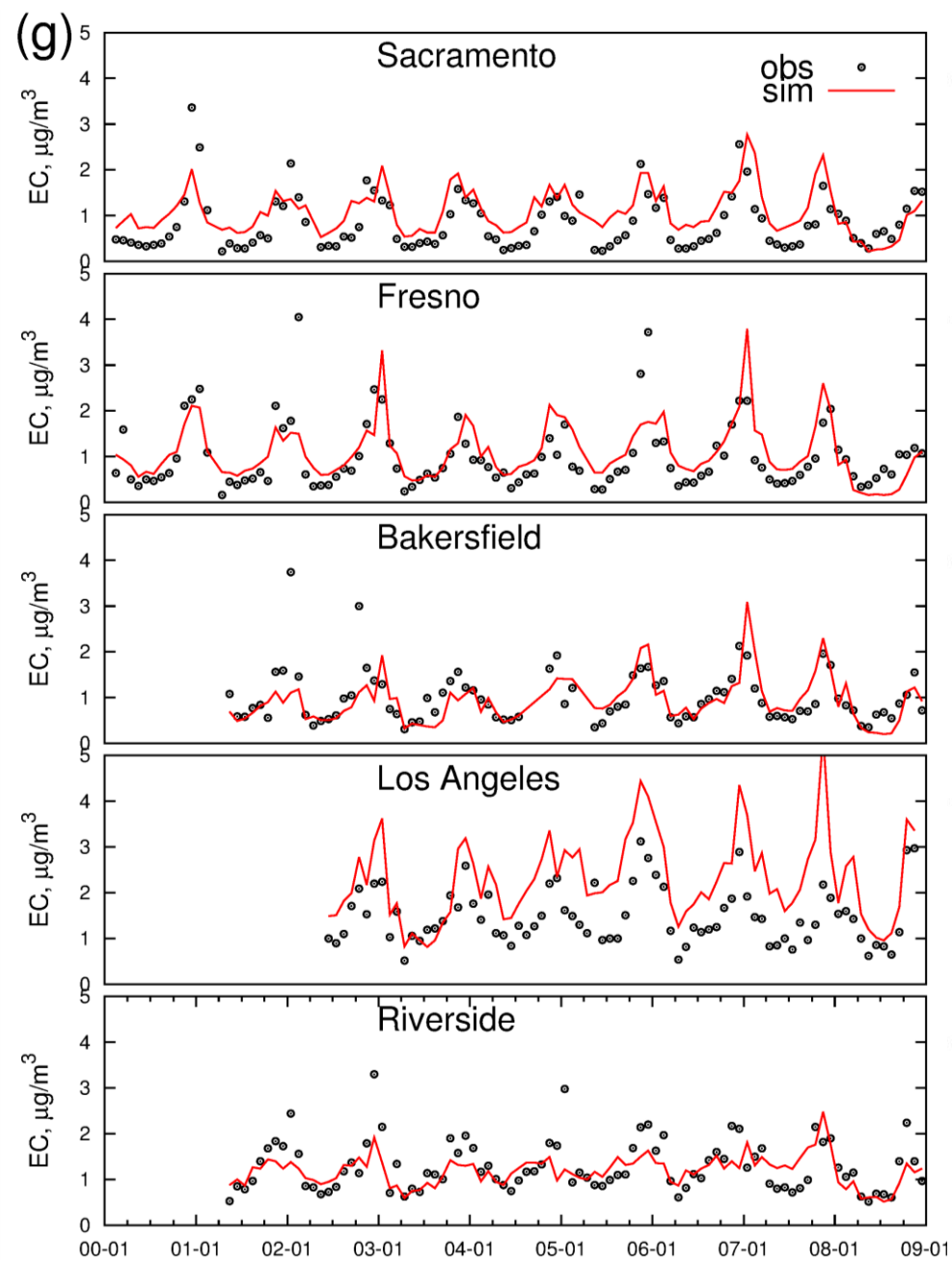
Predicted and Measured Concentrations
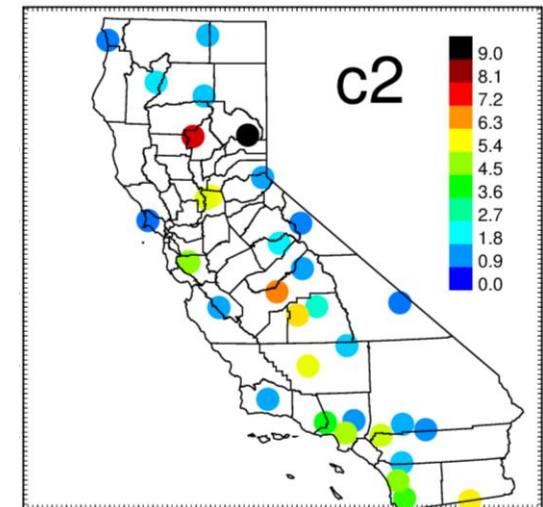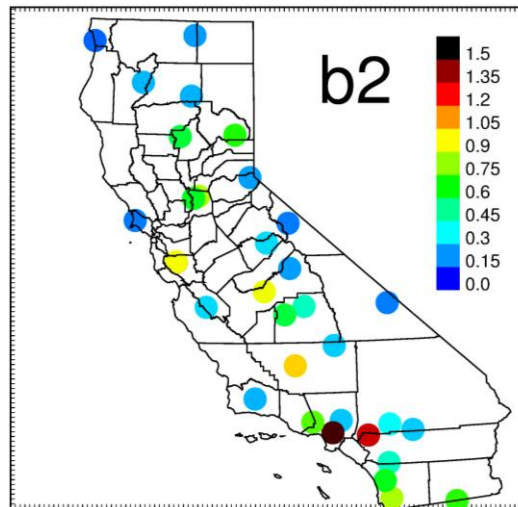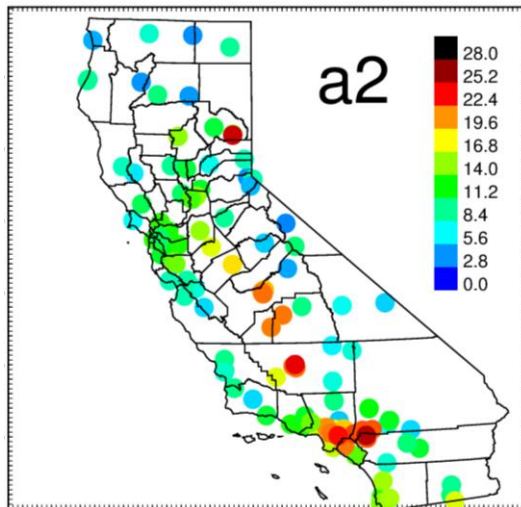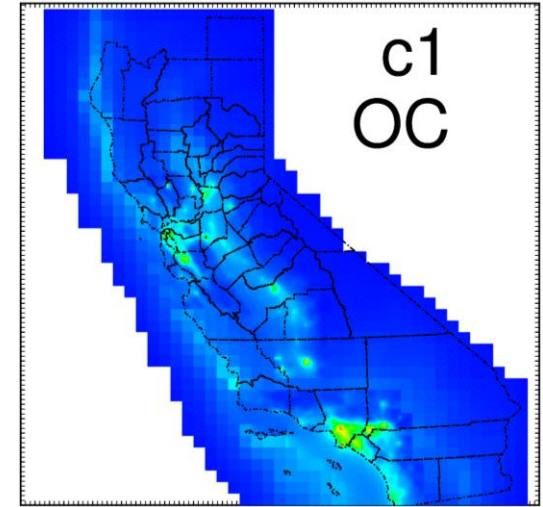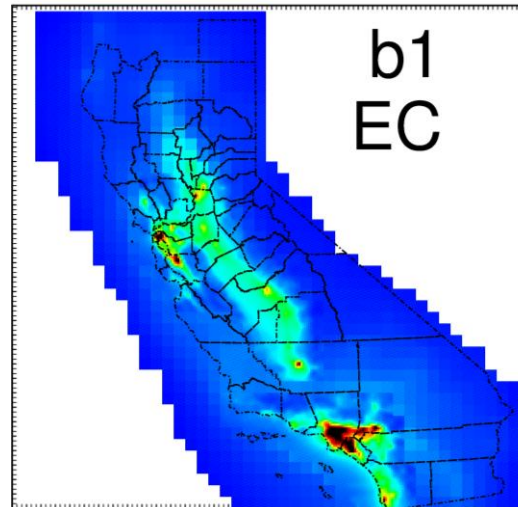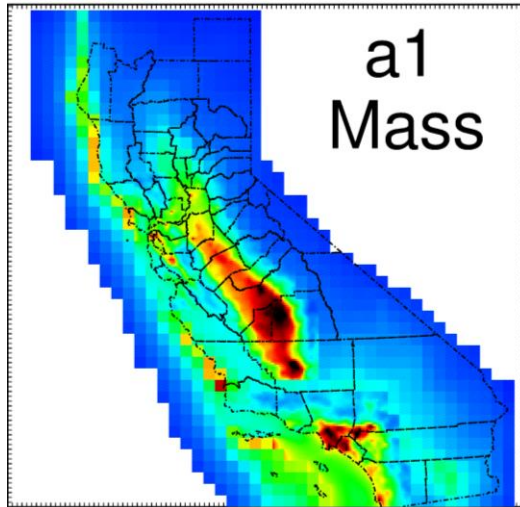
Predicted and Measured Concentrations
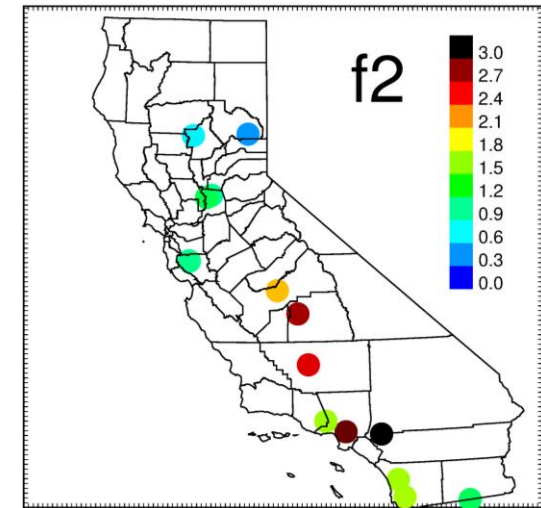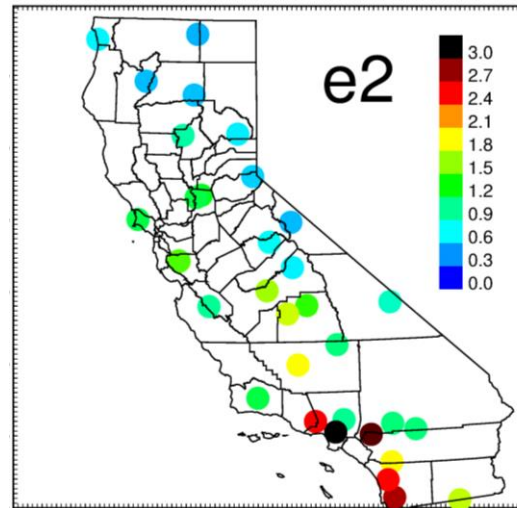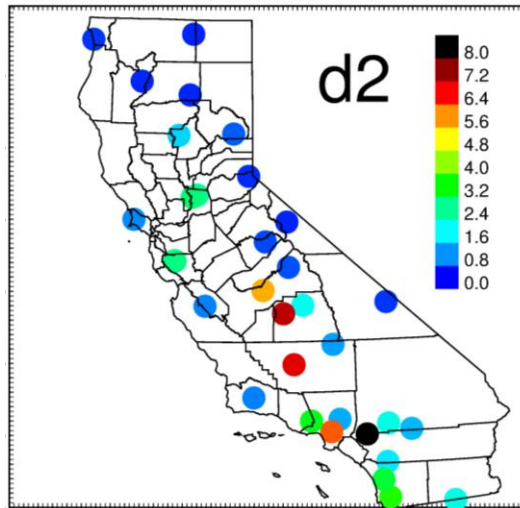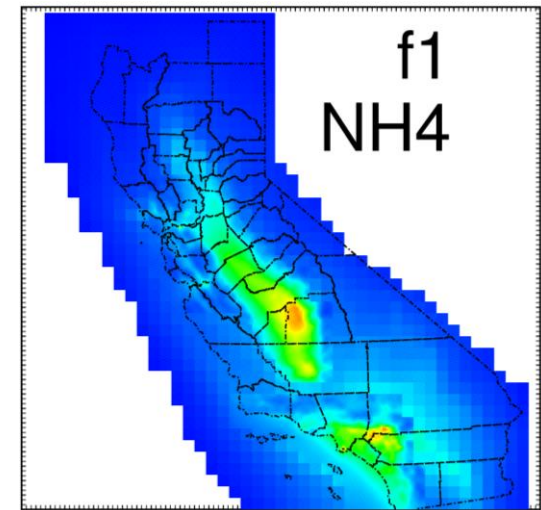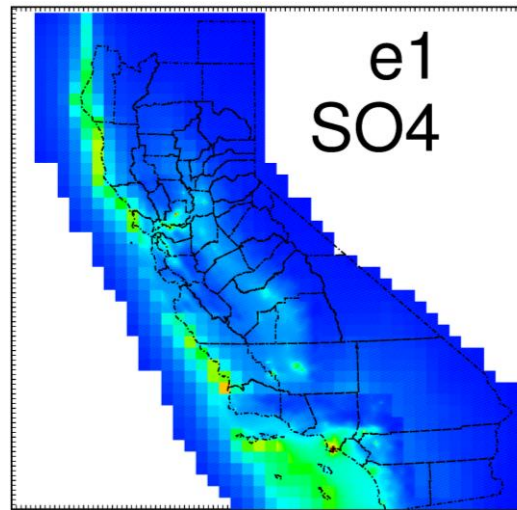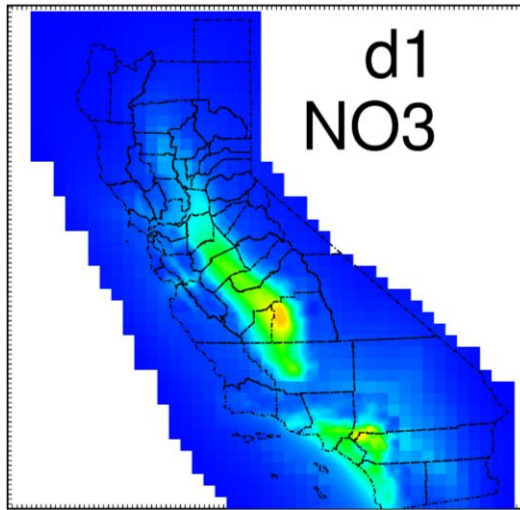
Organic Carbon Predictions vs. Measurements
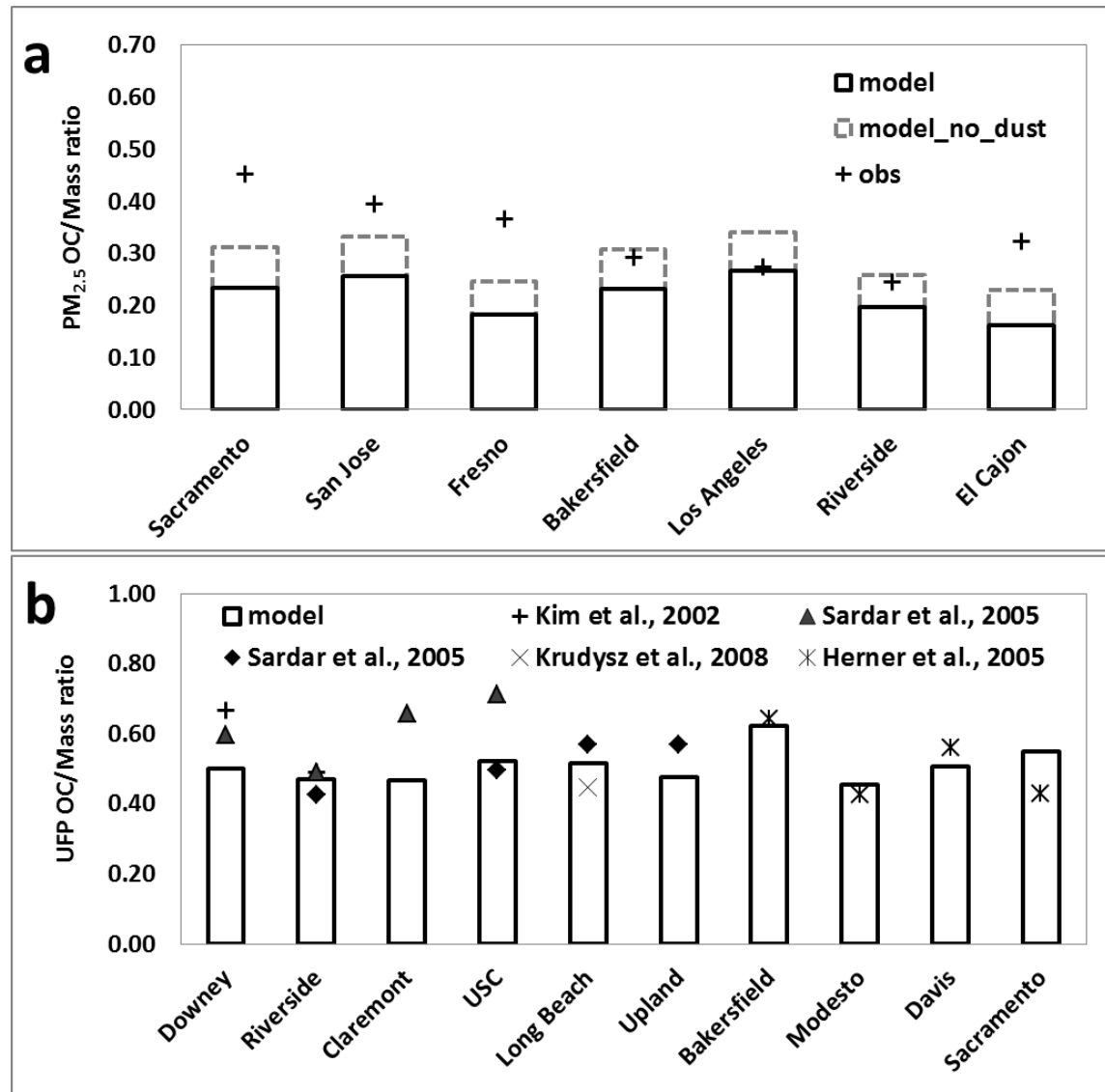
SOA Predictions vs. Measurements
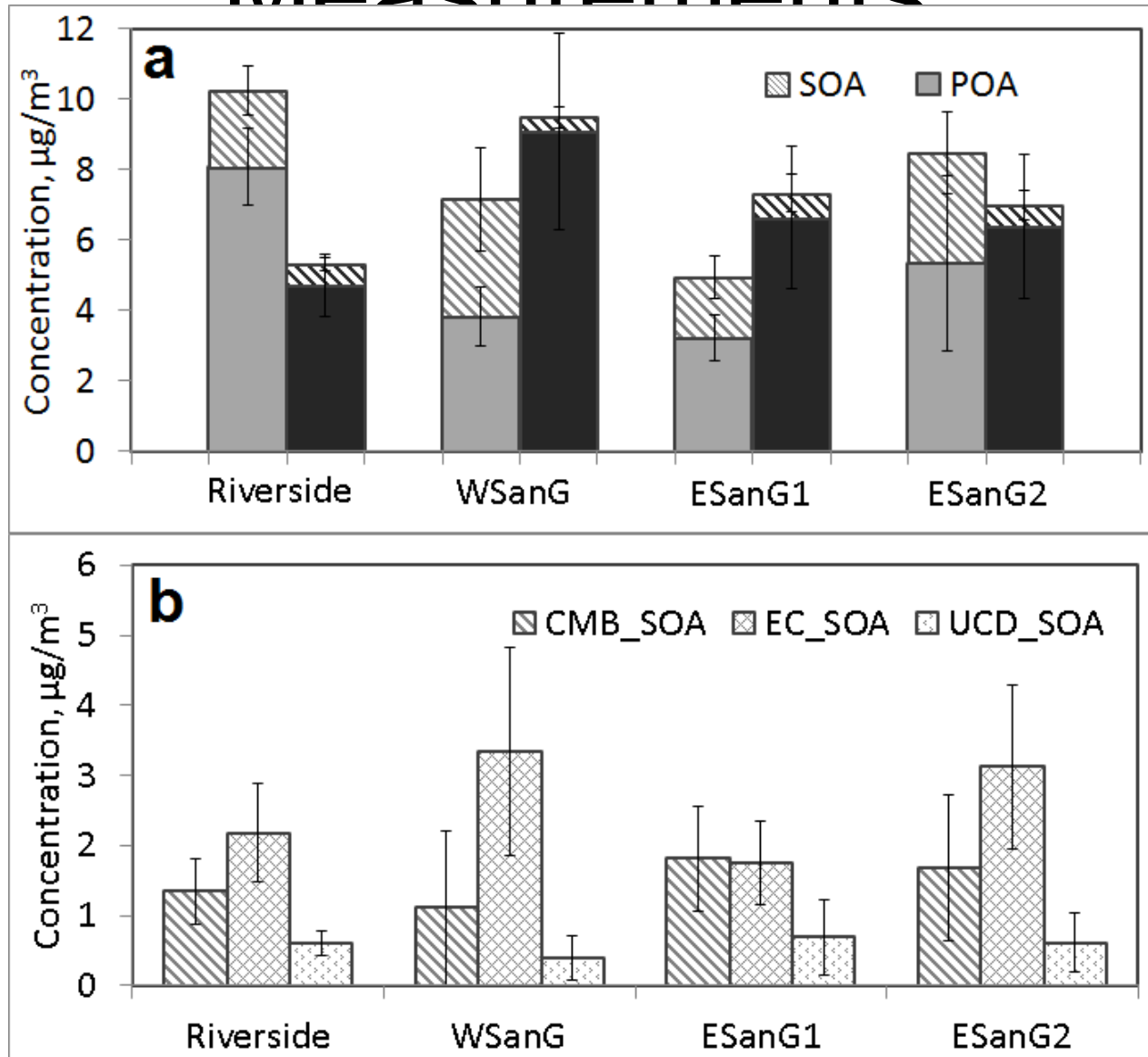
Predicted Sources of SOA

Predicted Sources of POA

a. Onroad gas — Max: 0.8
b. Offroad gas — Max: 0.4
c. Onroad die — Max: 0.4
d. Offroad die — Max: 1.2
e. Woodsmoke — Max: 4.0
f. MeatCooking — Max: 3.0
g. HighSulfur — Max: 0.5
h. Other Anth. — Max: 4.0
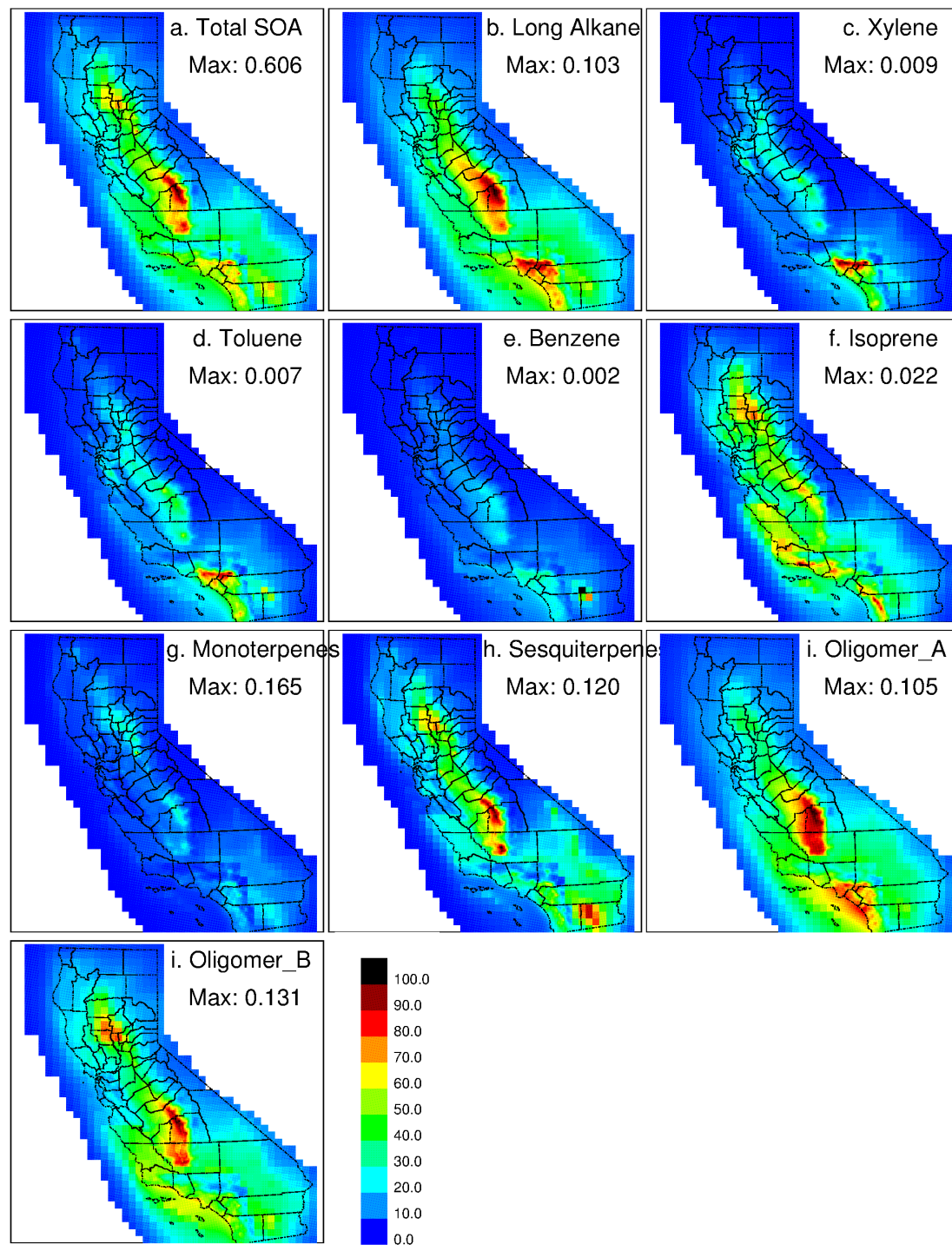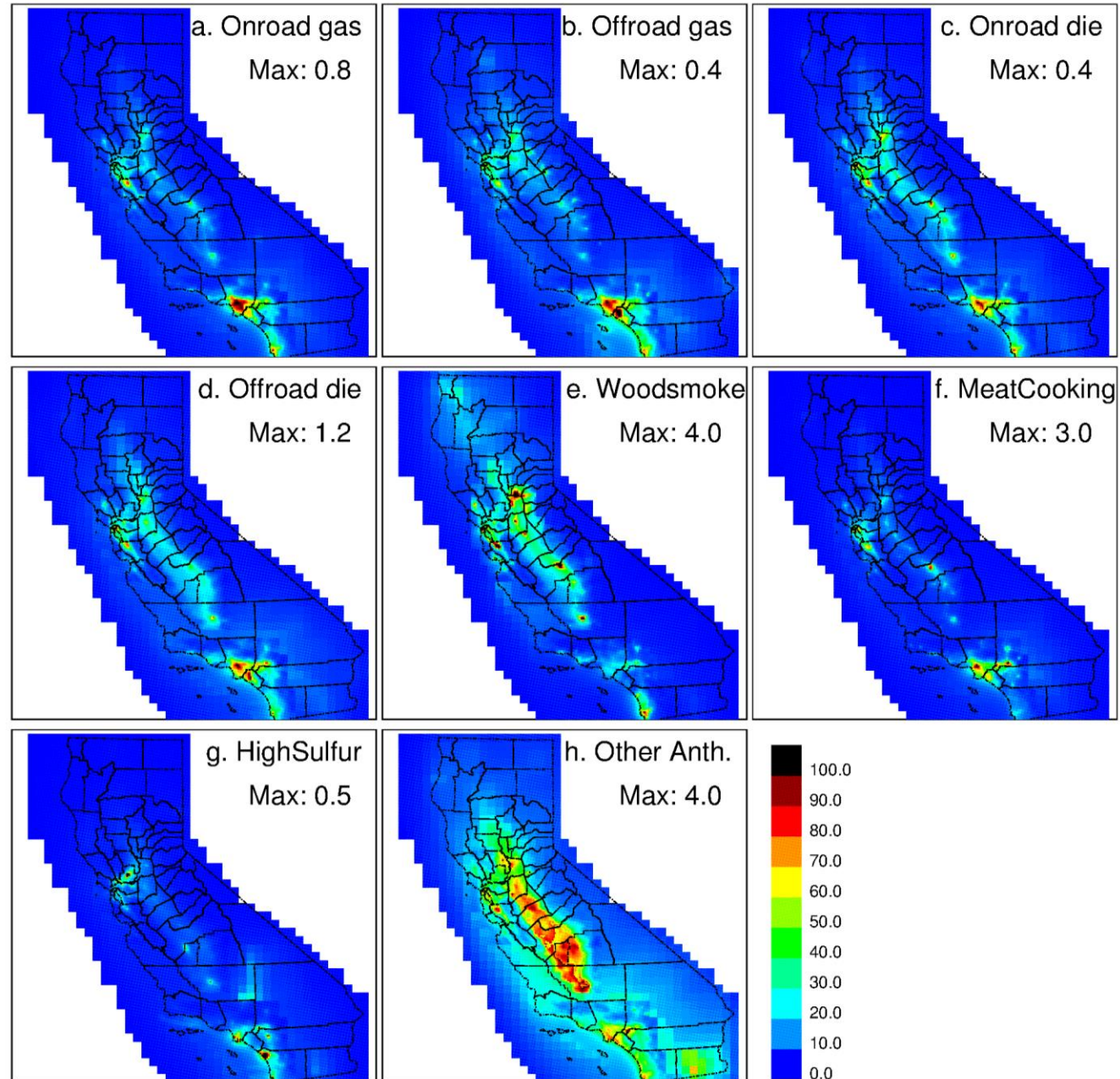
Seasonal Variation of Source Contributions to POA
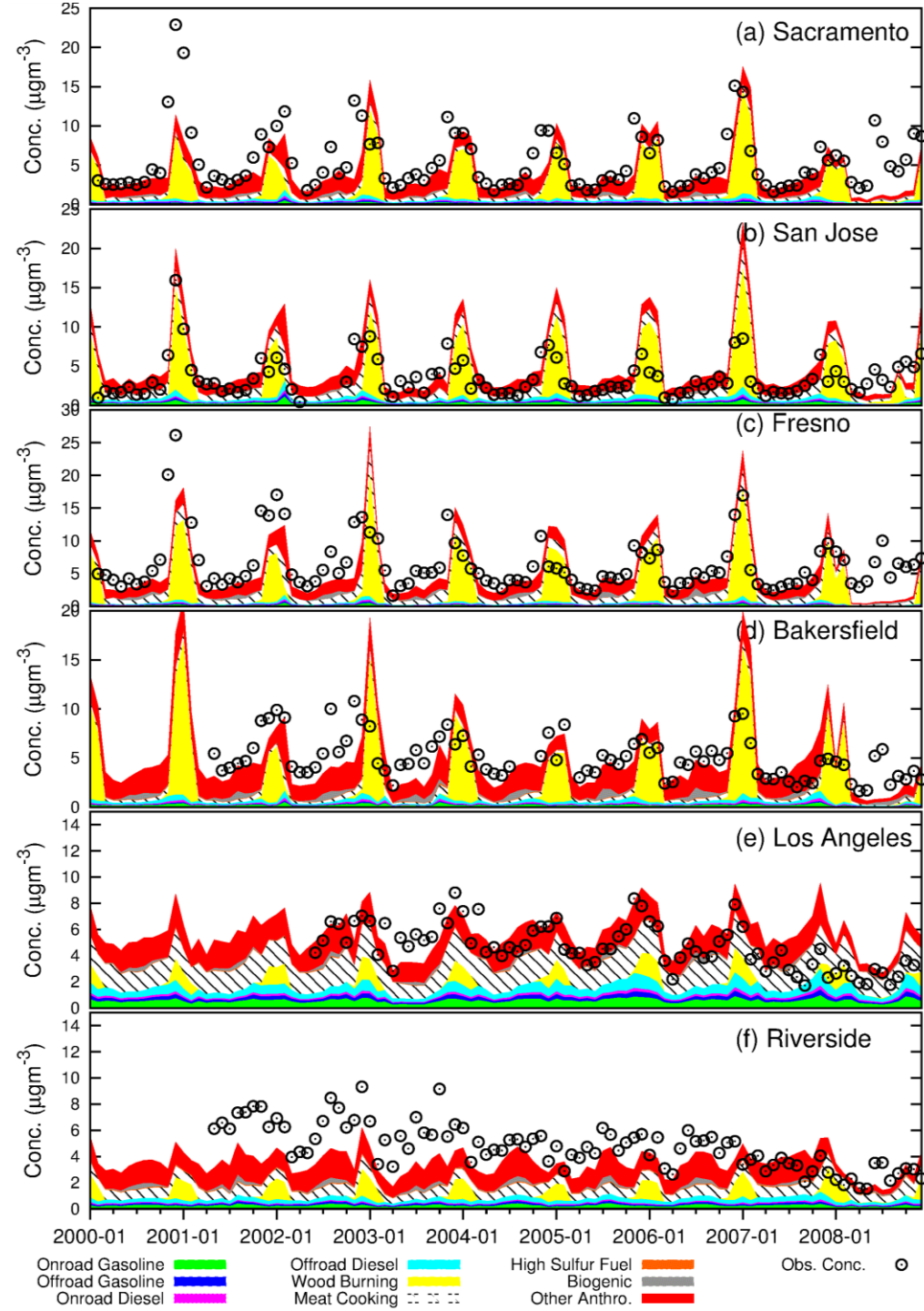
All Air Pollution Exposure Fields Available Free of Charge

- http://faculty.engineering.ucdavis.edu/kleeman/

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Task 2 Hypothesis 1

- Long-term (seasonal) residential exposures to TRAP in children with asthma increases risk of an asthma hospital encounter from short-term increases in ambient air pollution.

- **Rationale** (*vulnerability and susceptibility*)**:**
- Increased ambient air pollution may be accompanied by higher excursions in TRAP exposures at homes near busy traffic (<u>vulnerability</u>):
  - Surface temperature inversions and air stagnation are correlated with increased concentrations of air pollutants near ground level leading to higher risks of asthma admissions (Norris 2000 Thorax 55:466-70).
  - Homes near dense traffic are expected to be most affected under these conditions of air stagnation.
- Chronic TRAP exposure may increase <u>susceptibility</u> (e.g., chronic airway inflammation)

Task 2 Hypothesis 2

- Asthma morbidity will be additively associated with daily traffic-related air pollutant exposures near subject homes (CALINE4 and UCD/CIT primary pollutants) and UCD/CIT SOA and/or ambient O_3.

- **Rationale:** Primary and secondary air pollutants show low correlations and likely both induce oxidative stress and inflammatory responses in the lung.

Design Overview

- Case-crossover study design:

  - Each person acts as his or her own control. Subject characteristics are thus controlled for by design.

  - Subject characteristics are of interest as they may modify associations (Tasks 3-4) -- associations may be stronger in one group vs. another.

  - Exposures are sampled from the subject's time-varying distribution of exposure. Exposure at a time just prior to event (hospital encounter) is compared to exposures for a set of referent times for same days of week and 4-week period.

Population

- Hospital admissions and ED visits for a primary diagnosis of asthma (ICD-9-CM 493), subjects ages 0-18 years, 2000-2008

- Children's Hospital of Orange County and the University of California Irvine Medical Center

- Hospital catchment area -- urban core of Northern Orange County, California.

Demographic characteristics of the hospital data

Subject characteristics; %	Emergency Department visits (N = 8,088)	Hospital admissions (N = 3,089)	Total hospital encounters[a] (N =11,177)	Total unique subjects seen, (N =7,492)[b]
Male	63	61	63	62
Age (years)				
0-4	52	62	55	55
5-12	38	32	36	36
13-18	10	6	9	9
Race-ethnicity				
White non-Hispanic	36	35	36	36
White Hispanic	54	53	54	52
African American	3	4	3	3
Asian	3	4	3	4
Other/Unknown	4	4	4	5
Source of Payment				
Private Insurance[c]	36	41	37	38
Government Sponsored or Uninsured[d]	62	53	60	58
Unknown	2	6	3	4

Exposure summary

- Task 1 <u>weekly</u> average UCD/CIT Source Oriented Chemical Transport Model outputs of SOA and POA source contributions in three particle size fractions: ultrafine PM < 0.1 μm ($PM_{0.1}$), fine PM ($PM_{2.5}$), and fine plus coarse PM (PM_{10});

- Task 2: <u>weekly</u> average concentrations of residential traffic dispersion-modeled CO, NO_x, UFP and $PM_{2.5}$;

- <u>Six-month seasonal</u> concentrations of residential traffic dispersion-modeled CO, NO_x, UFP and $PM_{2.5}$:
  <u>warm season</u>: May-October;
  <u>cool season</u>: November-April

Exposures

- Residential addresses for each hospital encounter were geocoded (Tele Atlas).

- Linked each subject addresses to:
  - Nearest ambient monitoring station measurements from EPA's Air Quality System for daily $PM_{2.5}$, NO_2, NO_x, CO, O_3;
  - Nearest 4x4 km grid for the UCD/CIT data.

Exposures

- Traffic data for major roads and highways (Caltrans) were linked to home locations.

- CALINE4 dispersion model: estimated 7-day ave. and 6-month seasonal $PM_{2.5}$, NO_x ($NO + NO_2$), and particle number (~ultrafine particles, UFP) concentrations at each residence from local traffic emissions (gasoline vehicles and diesel trucks) within a **500** m and 1500 m radius.

- Land-use regression data for 7-day ave. NO_x (not discussed)

CAlifornia LINE Source Dispersion Model (CALINE4)

- Developed by California Dept. of Transportation

- Uses Gaussian plume model for "line sources"

- Accounts for mechanical and thermal turbulence caused by vehicle movement and hot exhaust
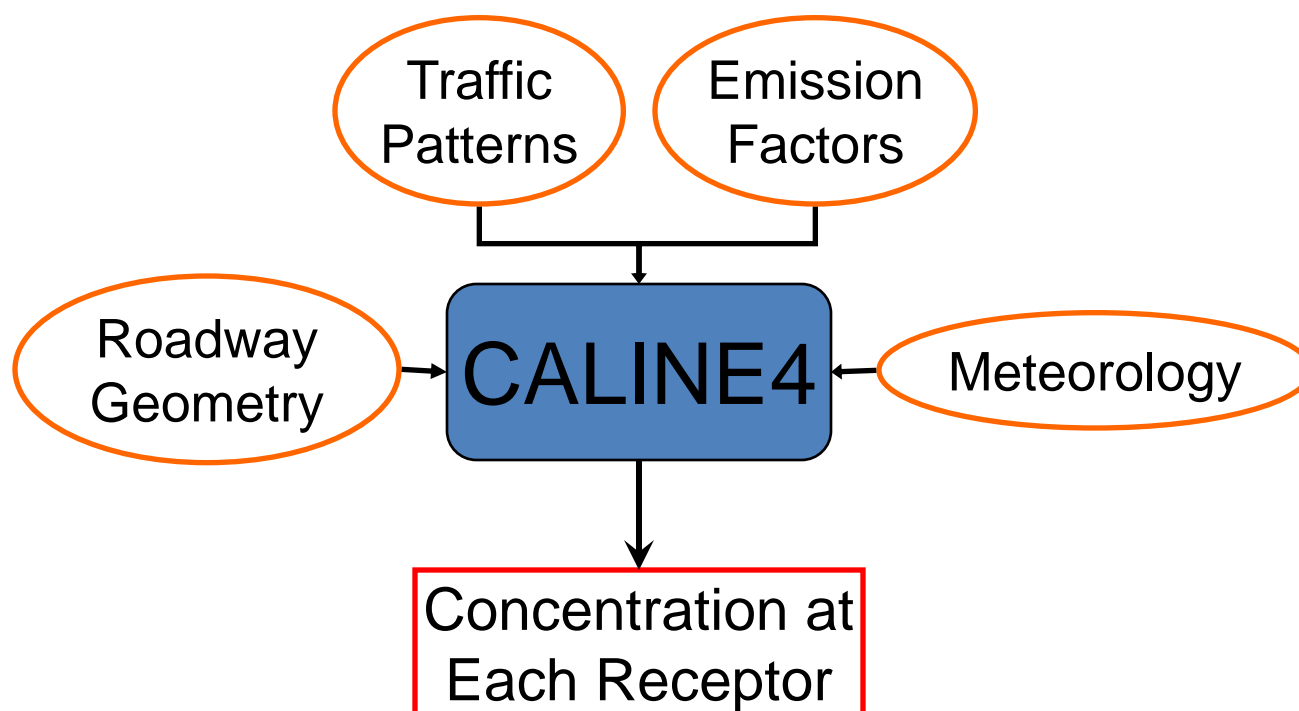
CALINE4 model

- Model inputs:

  - local traffic emissions of gasoline vehicles and diesel trucks within a 500 m radius buffer -- traffic volumes, roadway geometry, vehicle emission rates;

  - meteorology (wind speed, direction, and temperature).

- Emission factors for CO, NO_x, and $PM_{2.5}$ from the California Air Resources Board EMFAC2007 vehicle emissions model

- Emission factors for UFPs estimated based on traffic speed and the fraction of diesel trucks -- distance-dependant scaling functions developed and validated within CALINE4.

  (Yuan et al. 2011 Chemical Product and Process Modeling 6 (1): Article 8)

Traffic Inputs

- Traffic activities
  - Freeways and highways:
    - Annual average traffic count data on freeways and highways from Caltrans Performance Measurement System (PeMS).
    - Fleet composition from Weigh-in-Motion (WIM) data at key locations on selected freeways and highways (e.g. I-405, I-5, SR-91, and SR-57 in Orange County).
  - Surface streets: Caltrans annual average daily traffic counts (AADT).
  - Annual average freeway, highway and surface street data was scaled to diurnal and day-of-week traffic variation profiles on the freeway/highway or nearby freeway.

Validation of adjusted CALINE4 model using measurement data near (a) near I-405 and I-710 freeways in California; (b) FM-973 and I-35 freeways in Texas.
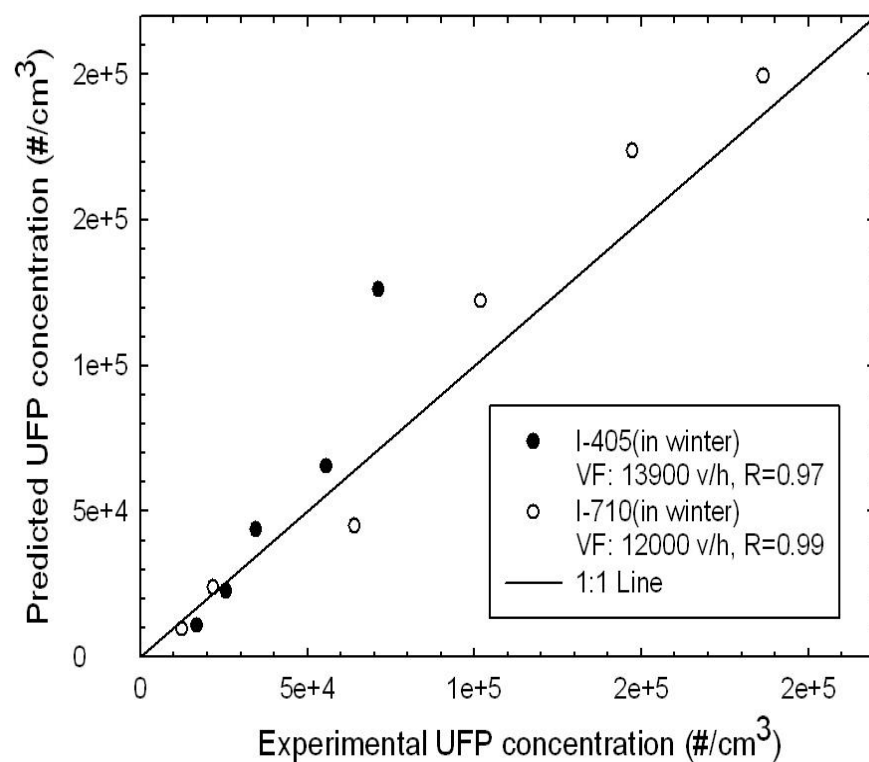
(a)
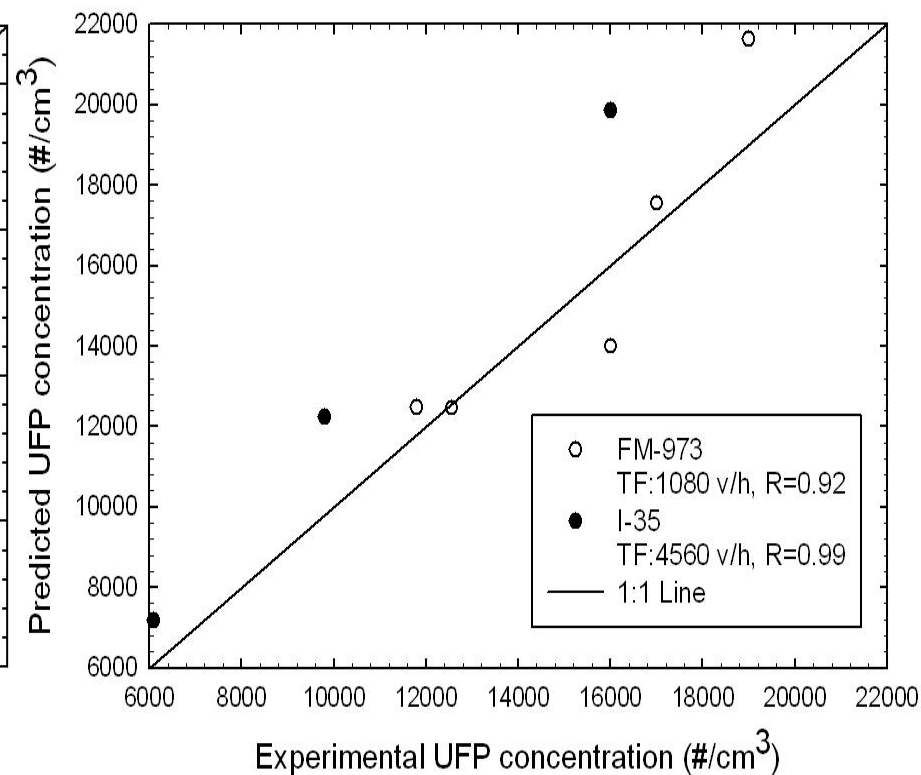
(b)

CALINE4 modeled (500 m buffer) NOx pollution surface by kriging the estimated nine-year average concentrations at the residences of the study subjects.
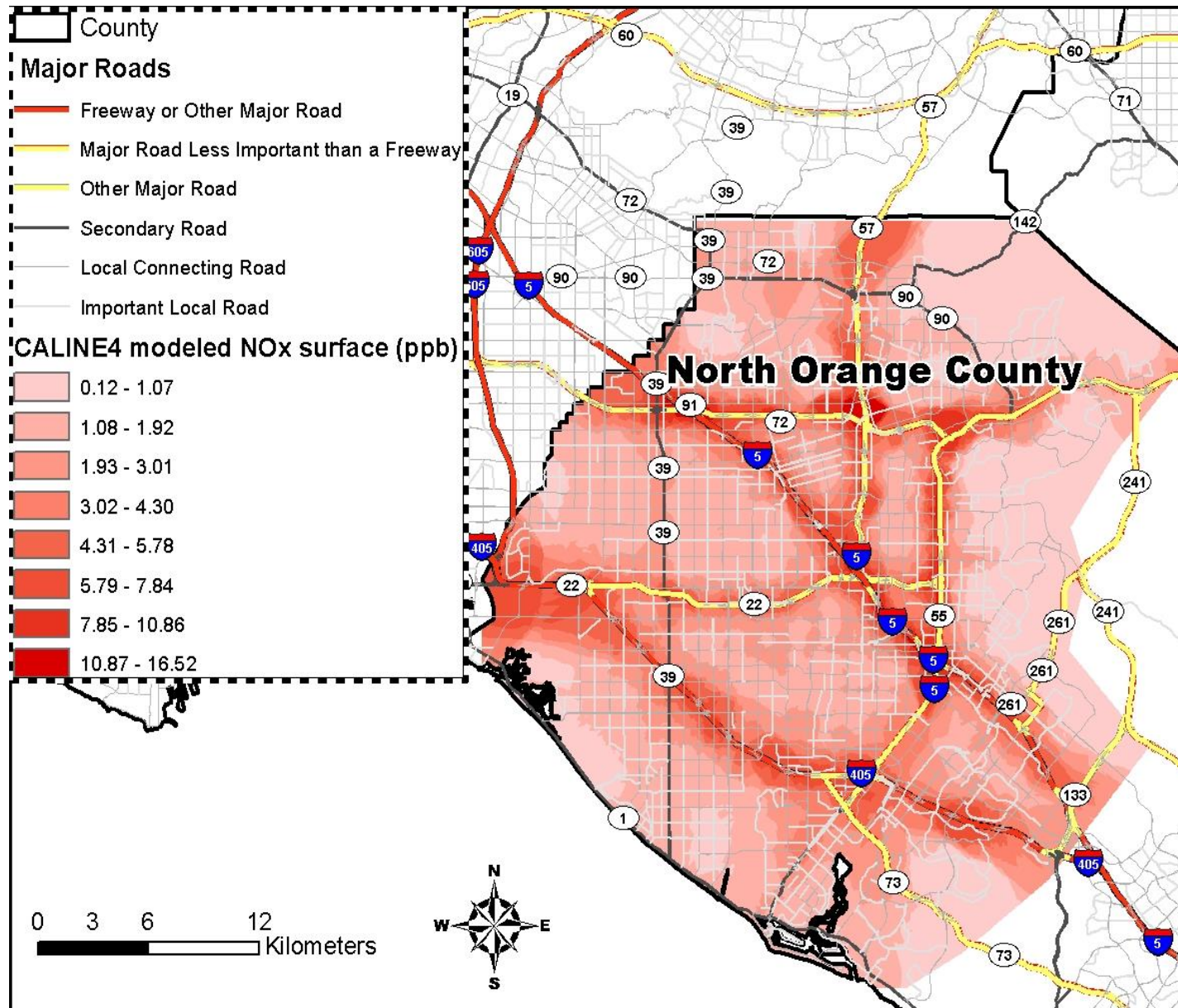
Analysis

- Case-crossover design -- parameter estimates obtained via conditional logistic regression

- Time invariant subject-specific characteristics (e.g. SES or race-ethnicity) are controlled for by design.

- Exposure 7 days prior to and including event date of the hospital encounter was compared to a set of referent times.

Semi-symmetric bidirectional referent selection
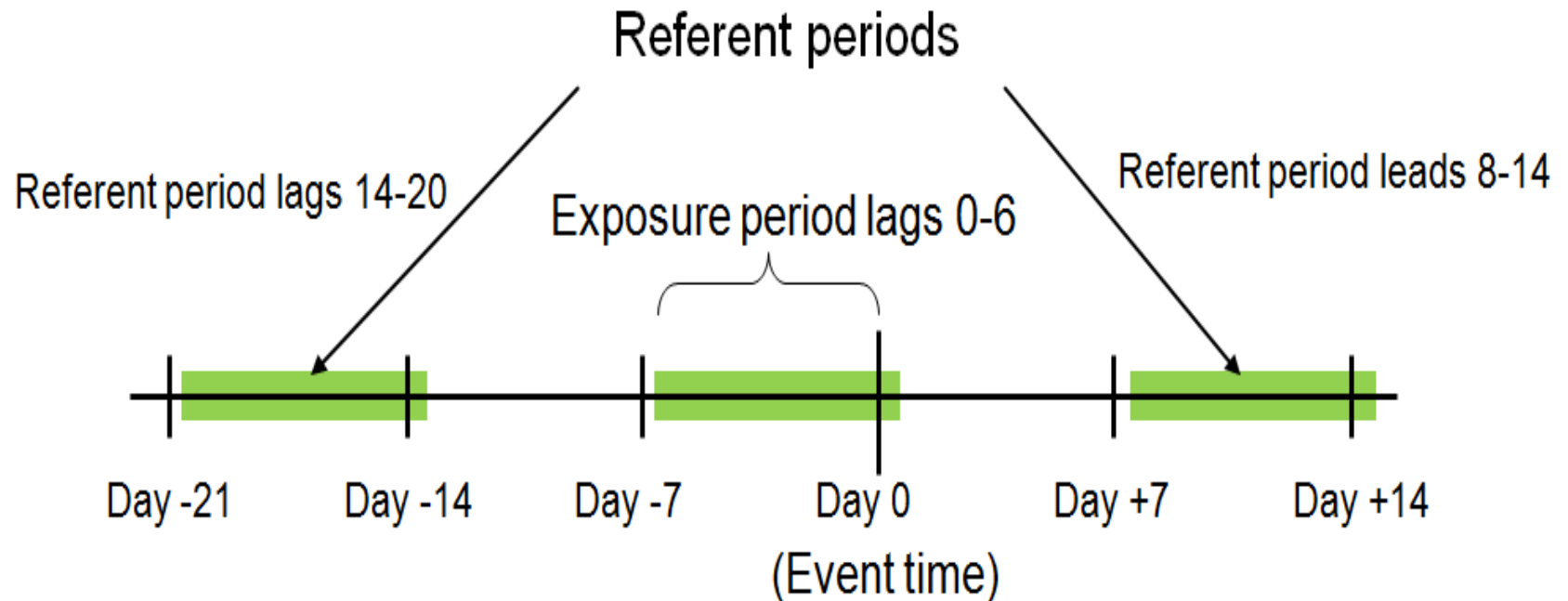
Janes H, Sheppard L, Lumley T. Epidemiology 2005;16:717-726

Analysis

- Referent periods were randomly selected.
  - Offset term used (1.6% of hospital encounters) if only one available referent or to avoid overlap bias (another encounter occurred within one of two referent periods.
  - This yields a localizable and ignorable design equivalent to the time-stratified method.

- Yields unbiased conditional logistic regression estimates and avoids bias resulting from exposure time trends (seasonal and day of week).

- Tested models stratified by season because of expected differences in unmeasured pollutant composition. O_3: presented only for warm season.

Analysis

- Tested regression estimates for current day ambient exposures (1-day), 3-day, 5-day and 7-day averages. 7-day for CALINE4 and UCD/CIT data.

- Models for ED visits and hospital admissions showed consistent effect estimates so the two asthma encounter types were combined.

- Adjusted for temperature and relative humidity of the same lag average as the air pollutants.

- To adjust for within-subject correlation from repeated hospital encounters, standard error of parameter estimates were obtained using robust variance estimator.

Analysis

- To test effect modification by 6-mo. seasonal average residential TRAP: subjects stratified above and below median CALINE4 exposures to provide sufficient sample size.

- Effect modification by TRAP assessed by product term interaction (significant at p-value < 0.1).

- Regression results standardized to interquartile range (IQR, 25th to 75th percentile) increase in each air pollutant to allow for comparisons.

Aim 2, Comparison of Pollutant Variables

- Compare associations of
  - UCD/CIT POA to SOA,
  - UCD/CIT ultrafine particle mass to accumulation and coarse mode particle mass,
  - UCD/CIT PM source contributions (e.g. diesel, gasoline, wood smoke, etc.),
  - CALINE4 traffic dispersion-modeled air pollutants to measurements of ambient air pollutants ($PM_{2.5}$ and criteria pollutant gases).

Aim 2, Comparison of Pollutant Variables

- <u>Multipollutant models</u>
  Evaluate the extent to which estimates of association with asthma morbidity in single pollutant models change in models with entries for two pollutants:

  - primary (combustion-related) air pollutants (UFP, POA, NO_x, and CO) are independent of secondary air pollutants (SOA or O_3).

  - $PM_{2.5}$ mass or O_3 are independent of SOA, particularly during the warm seasonal period.

  - $PM_{2.5}$ mass is independent of O_3.

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Effect Modification by Residential Traffic-Related Air Pollution

Ralph J. Delfino,[a] Jun Wu,[a,b] Thomas Tjoa,[a] Sevan K. Gullesserian,[c] Bruce Nickerson,[d] and Daniel L. Gillen[c]

Background: Ambient air pollution has been associated with asthma-related hospital admissions and emergency department visits (hospital encounters). We hypothesized that higher individual exposure to residential traffic-related air pollutants would enhance these associations.

Methods: We studied 11,390 asthma-related hospital encounters among 7492 subjects 0–18 years of age living in Orange County, California. Ambient exposures were measured at regional air monitoring stations. Seasonal average traffic-related exposures ($PM_{2.5}$, ultrafine particles, NO_x, and CO) were estimated near subjects' geocoded residences for 6-month warm and cool seasonal periods, using dispersion models based on local traffic within 500 m radii. Associations were tested in case-crossover conditional logistic regression models adjusted for temperature and humidity. We assessed effect modification by seasonal residential traffic-related air pollution exposures above and below median dispersion-modeled exposures. Secondary analyses considered effect modification by traffic exposures within race/ethnicity and insurance group strata.

Results: Asthma morbidity was positively associated with daily ambient O_3 and $PM_{2.5}$ in warm seasons and with CO, NO_x, and $PM_{2.5}$ in cool seasons. Associations with CO, NO_x, and $PM_{2.5}$ were stronger among subjects living at residences with above-median traffic-related exposures, especially in cool seasons. Secondary analyses showed no consistent differences in association, and 95% confidence intervals were wide, indicating a lack of precision for estimating these highly stratified associations.

Conclusions: Associations of asthma with ambient air pollution were enhanced among subjects living in homes with high traffic-related air pollution. This may be because of increased susceptibility (greater asthma severity) or increased vulnerability (meteorologic amplification of local vs. correlated ambient exposures).

S tudies have shown acute adverse changes in respiratory outcomes among children with asthma from short-term increases in exposure to ambient air pollutants, including particulate matter ≤2.5 mm ($PM_{2.5}$), ozone (O_3), and nitrogen dioxide (NO_2).[1] Among these are time series studies in which aggregate counts of emergency department visits or hospital admissions for asthma have been related to ambient air pollution measured at regional locations. Generally, all subjects in

Pediatric asthma hospital morbidity and ambient air pollution, cool season models: Effect modification by CALINE4 TRAP.

Pediatric asthma hospital morbidity and ambient air pollution, cool season models: Effect modification by CALINE4 TRAP.

Pediatric asthma hospital morbidity and ambient air pollution, cool season models: Effect modification by CALINE4 TRAP.

Pediatric asthma hospital morbidity and ambient air pollution, warm season models: Effect modification by CALINE4 TRAP.

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Pediatric asthma hospital morbidity and ambient air pollution, warm season models: Effect modification by CALINE4 TRAP.

Pediatric asthma hospital morbidity and ambient air pollution, warm season models: Effect modification by CALINE4 TRAP.

Associations between pediatric asthma hospital encounters and interquartile range increases in 7-day average residential TRAP estimated by CALINE4 models.

Air Pollutant	Warm Season, % change in risk (95% CI)	Cool Season, % change in risk (95% CI)
CALINE4 Dispersion model (500 m buffer)		
PM$_{2.5}$ (µg/m^3)	-2.88 (-14.85, 10.77)	**9.38 (1.59, 17.75)**
NO$_x$ (ppb)	-0.78 (-13.26, 13.48)	**9.94 (1.63, 18.93)**
Particle Number (no./cm^3)	-5.94 (-14.05, 2.94)	**8.75 (3.27, 14.51)**
CALINE4 Dispersion model (1500 m buffer)		
PM$_{2.5}$ (µg/m^3)	-12.32 (-29.47, 8.92)	**17.53 (4.57, 32.07)**
NO$_x$ (ppb)	-11.47 (-28.58, 9.68)	**17.03 (4.03, 31.64)**
Particle Number (no./cm^3)	-12.34 (-23.57, 0.51)	**12.24 (3.80, 21.37)**

Associations between pediatric asthma hospital encounters and interquartile range increases in 7-day average UCD/CIT-modeled primary and secondary organic aerosol: $PM_{0.1}$

Air Pollutant	Warm Season, % change in risk (95% CI)[a]	Cool Season, % change in risk (95% CI)
$PM_{0.1}$		
$PM_{0.1}$ SOA	-10.03 (-16.81, -2.70)	-3.93 (-14.28, 7.67)
$PM_{0.1}$ POA	-18.47 (-33.69, 0.10)	**19.38 (7.96, 32.00)**
$PM_{0.1}$ POA from on-road gasoline & diesel	-12.36 (-29.07, 8.19)	**25.32 (10.50, 42.09)**
$PM_{0.1}$ POA from off-road gasoline & diesel	-5.95 (-20.33, 11.02)	**18.94 (7.93, 31.06)**
$PM_{0.1}$ POA from woodsmoke	---	0.02 (-0.02, 0.05)
$PM_{0.1}$ POA from meat cooking	3.19 (-12.95, 22.32)	**18.64 (5.17, 33.80)**
$PM_{0.1}$ POA from high sulfur content fuel combustion	-8.35 (-19.28, 4.04)	**21.56 (6.04, 39.31)**
$PM_{0.1}$ POA from other anthropogenic sources	-20.59 (-32.02, -7.32)	**20.29 (8.42, 33.44)**

Associations between pediatric asthma hospital encounters and interquartile range increases in 7-day average UCD/CIT-modeled primary and secondary organic aerosol: PM$_{2.5}$

Air Pollutant	Warm Season, % change in risk (95% CI)[a]	Cool Season, % change in risk (95% CI)
PM$_{2.5}$		
PM$_{2.5}$ SOA	-3.71 (-12.14, 5.53)	**-16.80 (-29.63, -1.70)**
PM$_{2.5}$ POA	2.60 (-12.01, 19.63)	**14.99 (7.04, 23.53)**
PM$_{2.5}$ POA from on-road gasoline & diesel	10.21 (-6.34, 29.66)	**16.23 (6.41, 26.94)**
PM$_{2.5}$ POA from off-road gasoline & diesel	8.39 (-4.56, 23.10)	**12.39 (5.69, 19.50)**
PM$_{2.5}$ POA from woodsmoke	---	**4.21 (1.07, 7.44)**
PM$_{2.5}$ POA from meat cooking	**16.43 (1.75, 33.21)**	**13.59 (4.95, 22.94)**
PM$_{2.5}$ POA from high sulfur content fuel combustion	12.81 (-2.33, 30.28)	**13.53 (1.57, 26.89)**
PM$_{2.5}$ POA from other anthropogenic sources	-4.08 (-17.39, 11.38)	**19.38 (8.08, 31.85)**

Associations between pediatric asthma hospital encounters and interquartile range increases in 7-day average UCD/CIT-modeled primary and secondary organic aerosol: PM_{10}

Air Pollutant	Warm Season, % change in risk (95% CI)[a]	Cool Season, % change in risk (95% CI)
PM_{10}		
PM_{10} SOA	-1.31 (-10.11, 8.35)	**-18.95 (-31.12, -4.71)**
PM_{10} POA	4.59 (-10.12, 21.71)	**13.98 (6.42, 22.07)**
PM_{10} POA from on-road gasoline & diesel	8.63 (-7.81, 27.98)	**17.48 (7.32, 28.59)**
PM_{10} POA from off-road gasoline & diesel	7.43 (-5.46, 22.04)	**12.85 (6.05, 20.09)**
PM_{10} POA from woodsmoke	---	**4.31 (1.15, 7.56)**
PM_{10} POA from meat cooking	**15.28 (0.72, 31.92)**	**14.45 (5.58, 24.06)**
PM_{10} POA from high sulfur content fuel combustion	11.58 (-3.53, 29.03)	**14.91 (2.47, 28.86)**
PM_{10} POA from other anthropogenic sources	2.84 (-10.80, 18.56)	**14.76 (6.29, 23.89)**

Associations between pediatric asthma hospital encounters and interquartile range increases in 7-day average UCD/CIT-modeled POA (% change in risk, 95% CI): differences by PM size fraction in the cool season.

	$PM_{0.1}$	$PM_{2.5}$	PM_{10}
POA	**19.38 (7.96, 32.00)**	14.99 (7.04, 23.53)	13.98 (6.42, 22.07)
POA from on-road gasoline & diesel	**25.32 (10.50, 42.09)**	16.23 (6.41, 26.94)	17.48 (7.32, 28.59)
POA from off-road gasoline & diesel	**18.94 (7.93, 31.06)**	12.39 (5.69, 19.50)	12.85 (6.05, 20.09)
POA from wood smoke	0.02 (-0.02, 0.05)	**4.21 (1.07, 7.44)**	**4.31 (1.15, 7.56)**
POA from meat cooking	**18.64 (5.17, 33.80)**	13.59 (4.95, 22.94)	14.45 (5.58, 24.06)
POA from high sulfur content fuel combustion	**21.56 (6.04, 39.31)**	13.53 (1.57, 26.89)	14.91 (2.47, 28.86)
POA from other anthropogenic sources	**20.29 (8.42, 33.44)**	**19.38 (8.08, 31.85)**	14.76 (6.29, 23.89)

Two-pollutant models: PM$_{2.5}$ and O$_3$, warm season
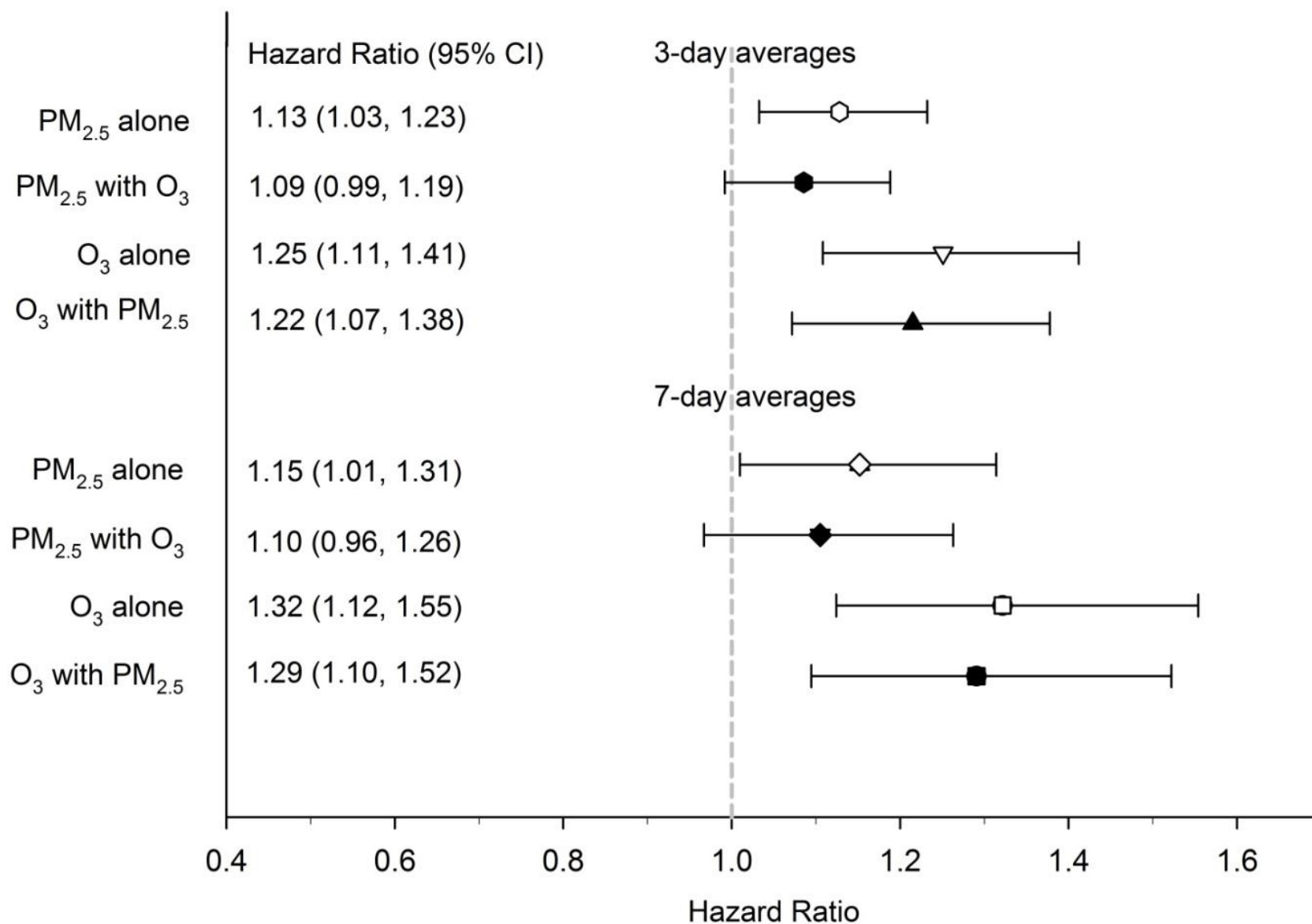
Two-pollutant models

- The warm season association with 7-day ave. ambient $PM_{2.5}$ was either unchanged or increased when co-regressed with 7-day CALINE4 TRAP, UCD/CIT SOA and POA or ambient primary gases (NO_2, NO_x and CO).

- However, cool-season ambient $PM_{2.5}$ was negatively confounded by UCD/CIT POA, CALINE4 TRAP and ambient primary gases.

- Warm season association of asthma with ambient O_3 was not confounded by UCD/CIT SOA or POA, CALINE4 TRAP, or ambient primary gases.

Task 2 Conclusions

- Positive associations of asthma morbidity with ambient CO, NO_2, NO_x, and $PM_{2.5}$, particularly during the colder seasons, is enhanced among subjects living in areas with high TRAP near the home (500 m).

- Associations in time-series studies may thus underestimate effects of ambient air pollutants on asthma morbidity for vulnerable populations exposed to high TRAP.

- Positive associations of asthma morbidity with ambient O_3 in the warm season is enhanced among subjects living in areas with <u>low</u> TRAP near the home (500 m):
  possible reason: $NO + O_3 \rightarrow NO_2 + O_2$

Task 2 Conclusions

- Both 7-day average CALINE4 TRAP and UCD-CIT POA are positively associated with of asthma hospital encounters in the cool but not warm season (except meat cooking POA).

- 7-day average CALINE4 particle number and $PM_{2.5}$ in the cool season were similarly associated with asthma morbidity for exposures estimated at 500 m radius buffers. Associations for both exposures were stronger at 1500 m.

- UCD-CIT ultrafine POA for most sources except wood smoke were more strongly associated with asthma morbidity than $PM_{2.5}$ or PM_{10}, although CIs overlapped considerably.

Task 2 Conclusions

- Positive associations for meat cooking POA were of similar magnitude to other sources.

  Possible reasons: influence of meteorology that leads to parallel model predictions -- correlations of total POA as well as gasoline and diesel sources with meat cooking was >0.8 for all size fractions.

  Note: meat cooking POA in $PM_{2.5}$ and PM_{10} were the only source contributions significantly associated with asthma encounters in the warm season.

- Verma et al. Environ Sci Technol. 2015 Mar 6. [Epub]: Cooking OA had relatively high DTT activity.

Task 2 Conclusions: Multipollutant Models

- Two-pollutant models of warm season ambient O_3 and $PM_{2.5}$ show marked independence of associations consistent with the New York study by Silverman and Ito (J Allergy Clin Immunol. 2010;125:367-373.e5).

- Two-pollutant models in the **cool season** supported expectations that UCD/CIT POA, CALINE4 TRAP, and primary gases are representative of causal primary PM components that are not adequately captured by $PM_{2.5}$ mass.

- In contrast, the association with **warm season** $PM_{2.5}$ mass is independent of above markers of primary combustion products (most were not significant), suggesting an unmeasured set of PM characteristics. SOA?

Outline

- Background
  - Epidemiologic research of acute asthma and air pollution
  - Data gaps / Exposure assessment
- Overview of Study
- Task 1
- Task 2
  - Introduction and Methods
  - Results
- Task 3
  - **Introduction and Methods**
  - Results
- Task 4
  - Introduction and Methods
  - Results
- Overall Conclusions and Discussion

Task 3 Hypothesis

- Associations observed in Task 2 will be strongest among subjects with multiple hospital encounters, which may be considered an indicator of greater asthma severity.

- Importance: decreasing repeated utilization of hospital resources through improvements in local air quality will improve public health and preserve health care resources.

Risk of repeated hospital encounters for asthma from chronic exposure to traffic-related air pollution

CALINE4 dispersion models used to estimate TRAP near homes of 2768 subjects ages 0-18 yrs, Orange County, CA, 2000-2003.

Exposure	Adjusted hazard ratio [a] (95% confidence interval) for an IQR increase in exposure	p-value
NO_2	1.042 (0.987, 1.101)	0.135
NO_x	1.097 (1.034, 1.164)	0.002
CO	1.073 (1.013, 1.137)	0.017

[a] Adjusted for sex, age group, race, health insurance status, distance to hospital, and poverty.

Delfino et al. *Ann Allergy Asthma Immunol.* 2009;102:138–144

Task 3

- Case-crossover analysis of subjects stratified based on recurrence of hospital encounters in order to assess whether children with multiple encounters show stronger associations with air pollutants.

- To reduce the likelihood of hospital usage outside of the study hospitals, subjects were selected from a 15-km catchment area (83% of population) around the 2 hospitals.

- Compare associations for 4,823 subjects with only one hospital encounter to associations for 1,777 subjects with more than one hospital encounter (N = 5,299 total encounters).
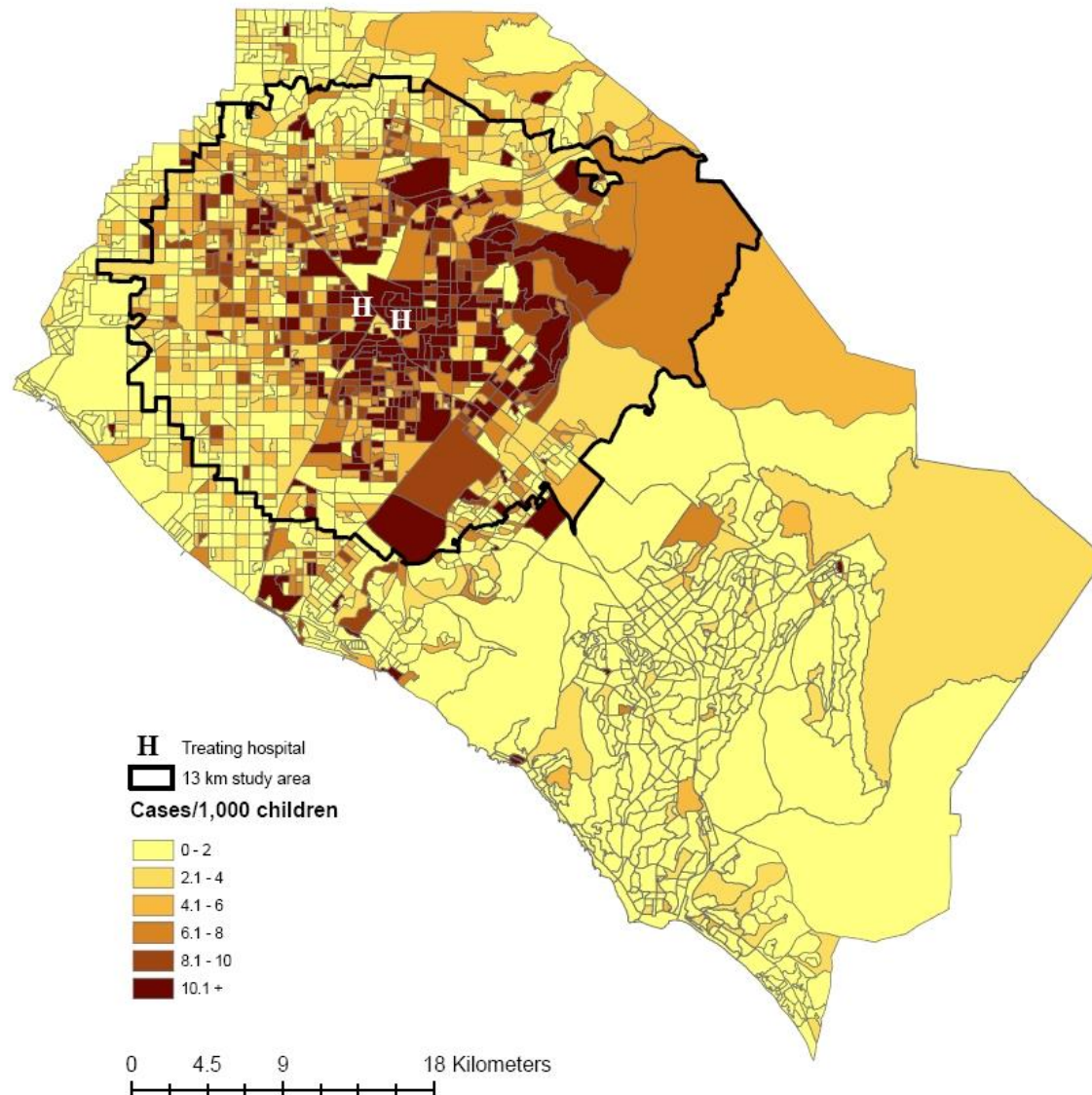
Children diagnosed with asthma for Emergency Department visits or hospitalizations at UCIMC and CHOC hospitals, 2000-2003: Number of subjects by census block group population (per 1,000).

Outline

- Background
  - Epidemiologic research of acute asthma and air pollution
  - Data gaps / Exposure assessment
- Overview of Study
- Task 1
- Task 2
  - Introduction and Methods
  - Results
- Task 3
  - Introduction and Methods
  - **Results**
- Task 4
  - Introduction and Methods
  - Results
- Overall Conclusions and Discussion

Associations between pediatric asthma hospital encounters and air pollution, warm season: effect modification by recurrence of encounters.

Ambient Air Pollutant	Lag-Day Average	Warm Season Odds Ratio (95% CI)[a]		Interaction p-value
		Repeated Encounters (N=2158)	No Repeated Encounters (N=2120)	
PM$_{2.5}$ 24-hr average	1-day	1.08 (0.99, 1.17)	1.07 (0.99, 1.16)	0.936
	3-day	**1.10 (1.00, 1.21)**	1.06 (0.98, 1.14)	0.558
	5-day	**1.14 (1.01, 1.28)**	1.02 (0.92, 1.13)	0.161
	7-day	1.14 (0.99, 1.30)	1.01 (0.90, 1.14)	0.212
O$_3$ 24-hr average	1-day	1.15 (0.98, 1.36)	1.11 (0.96, 1.29)	0.734
	3-day	**1.24 (1.01, 1.51)**	**1.22 (1.01, 1.46)**	0.905
	5-day	**1.33 (1.06, 1.68)**	1.22 (0.99, 1.51)	0.581
	7-day	**1.35 (1.03, 1.75)**	**1.32 (1.04, 1.68)**	0.930
NO$_x$ 24-hr average	1-day	0.90 (0.73, 1.10)	1.02 (0.84, 1.23)	0.379
	3-day	1.10 (0.84, 1.44)	1.04 (0.80, 1.36)	0.790
	5-day	1.04 (0.76, 1.44)	0.93 (0.68, 1.28)	0.626
	7-day	1.01 (0.70, 1.46)	0.83 (0.58, 1.19)	0.452
CALINE4 PM$_{2.5}$ 1500m	7-day	0.70 (0.49, 1.01)	0.99 (0.73, 1.33)	0.153
UCD/CIT PM$_{2.5}$ SOA	7-day	1.00 (0.87, 1.14)	0.91 (0.79, 1.04)	0.336
UCDCIT PM$_{2.5}$ POA	7-day	1.09 (0.86, 1.39)	0.94 (0.75, 1.18)	0.376

Associations between pediatric asthma hospital encounters and air pollution, cool season: effect modification by recurrence of encounters.

Ambient Air Pollutant	Lag-Day Average	Cool Season Odds Ratio (95% CI)		Interaction p-value
		Repeated Encounters (N=2689)	No Repeated Encounters (N=2703)	
PM$_{2.5}$ 24-hr average	1-day	1.04 (0.99 1.09)	1.03 (0.98, 1.08)	0.836
	3-day	1.03 (0.98 1.09)	1.04 (0.98, 1.10)	0.848
	5-day	**1.07 (1.00 1.14)**	1.06 (0.99, 1.14)	0.945
	7-day	**1.10 (1.03 1.19)**	**1.10 (1.01, 1.19)**	0.885
O$_3$ 24-hr average	1-day	0.81 (0.70 0.94)	0.95 (0.82, 1.09)	0.140
	3-day	0.68 (0.57 0.82)	0.92 (0.77, 1.10)	0.023
	5-day	0.60 (0.48 0.74)	0.76 (0.62, 0.94)	0.116
	7-day	0.57 (0.45 0.72)	0.71 (0.56, 0.90)	0.191
NO$_x$ 24-hr average	1-day	1.00 (0.94, 1.06)	1.01 (0.94, 1.08)	0.814
	3-day	1.06 (0.98, 1.15)	1.03 (0.95, 1.12)	0.678
	5-day	**1.13 (1.03, 1.25)**	1.09 (0.98, 1.20)	0.562
	7-day	**1.18 (1.06, 1.32)**	1.10 (0.98, 1.23)	0.381
CALINE4 PM$_{2.5}$	7-day	**1.25 (1.05, 1.47)**	1.08 (0.91, 1.28)	0.246
UCD/CIT PM$_{2.5}$ SOA	7-day	0.82 (0.64, 1.06)	0.87 (0.67, 1.14)	0.730
UCDCIT PM$_{2.5}$ POA	7-day	**1.20 (1.08, 1.34)**	**1.11 (1.00, 1.23)**	0.295

Task 3 Conclusions

- Limited evidence for a difference in association between asthma encounters and air pollutant exposures in subjects with vs. without recurrence of hospital encounters.

- Some cool season regression models (CALINE4, UCDCIT POA) suggested increased risk among the population with repeated visits to hospital, but interactions were nonsignificant.

Outline

- Background
  - Epidemiologic research of acute asthma and air pollution
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- Overview of Study
- Task 1
- Task 2
  - Introduction and Methods
  - Results
- Task 3
  - Introduction and Methods
  - Results
- Task 4
  - **Introduction and Methods**
  - Results
- Overall Conclusions and Discussion

Task 4 Hypothesis

- Associations observed in Task 2 will be strongest among subjects without health insurance or with government-sponsored insurance and strongest among those living in Census block groups with lower SES.

  - These factors are expected to increase risk as a result of limited access to health care, environmental factors and psychosocial stressors in poorer communities.

- Racial-ethnic differences in association, if any, may be in part due to these differences in SES.

Task 4 Methods

- Case-crossover models with product terms ($p < 0.1$ significant):
  - To assess effect modification of associations by subject socioeconomic characteristics;
  - To evaluate differences in association by race-ethnicity, sex, and pediatric age group.

- Three-way interaction models to test whether differences in associations between asthma and ambient air pollutants by seasonal residential CALINE4 TRAP could be due to **demographic characteristics** correlated with TRAP:
  Ambient air pollutant X CALINE4 strata X Demographic strata

  - Rationale: residential TRAP strata may be functioning as a surrogate of demographic differences that vary with traffic even though fixed subject characteristics cannot confound associations in the case-crossover models.

Task 4 Methods: SES

- <u>Health insurance</u>: private insurance vs. all others as a surrogate of lower SES (Cal-Optima, Medi-Cal, county funded insurance, other government, indigent, and self-pay).

- <u>Yost index</u>: Synthesis of 3 domains of SES (education, income and occupation, and cost of living).

  - From a principal components analysis from 7 Census SES variables (education index, median household income, percent living 200% below poverty level, percent blue-collar workers, percent ages >16 years in workforce without job, median rent, and median house value).

  - Dichotomized -- lower Yost score is the lower half of SES.

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  - Data gaps / Exposure assessment
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- Task 1
- Task 2
  - Introduction and Methods
  - Results
- Task 3
  - Introduction and Methods
  - Results
- Task 4
  - Introduction and Methods
  - **Results**
- Overall Conclusions and Discussion

Task 4 Results

- CALINE4 TRAP levels in both seasons were higher in Hispanic and African American subjects and in subjects without private insurance.

- Associations with ambient CO and NO_x in the cool season were stronger among Hispanics compared with non-Hispanic whites.

- Associations with ambient $PM_{2.5}$ in the warm season were stronger among subjects without vs. with private health insurance.

- Associations with ambient $PM_{2.5}$ in the warm and cool seasons were stronger among subjects living in neighborhoods with lower Yost scores (lower SES).

Task 4 Results

- Associations were stronger for subjects ages $\geq$12 years as compared with ages 0-11 years for $PM_{2.5}$, NO_2 and CO in both seasons, but product terms at $p < 0.1$ only for cool season $PM_{2.5}$.

- Several air pollutants were more strongly associated with asthma among females, but the difference was rarely statistically significant.

- 3-way interaction models of differences in associations of asthma with ambient air pollution by 6-month average CALINE4 residential TRAP were largely similar across demographic groups, but for nearly all 240 subgroups, 95% confidence intervals were wide.

Task 4 Conclusions

- Vulnerability due to higher exposures and demographic susceptibility is supported by our findings that:

  - Hispanic and African American subjects and subjects without private insurance were more likely to live in residences with higher dispersion-modeled TRAP.

  - Associations with several ambient air pollutants were stronger in Hispanics, subjects living in lower SES neighborhoods, and subjects without private insurance.

Task 4 Conclusions

- 3-way interaction: CALINE4 TRAP strata are not acting as surrogates of racial-ethnic or health insurance differences in studied geographic areas.

- However, smaller sample sizes of these highly stratified subgroups likely limited the statistical power.

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  - Data gaps / Exposure assessment
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- Task 1
- Task 2
  - Introduction and Methods
  - Results
- Task 3
  - Introduction and Methods
  - Results
- Task 4
  - Introduction and Methods
  - Results
- **Overall Conclusions and Discussion**

Overall Conclusions

- Associations of asthma hospital encounters with ambient CO, NO_2, NO_x, and $PM_{2.5}$, particularly during the colder seasons, is enhanced among subjects living in areas with high TRAP near the home (500 m).

- This finding includes subjects without private insurance and Hispanic and African American subjects, who may be at greater risk.

- Associations in time-series studies may underestimate effects of ambient air pollutants on asthma morbidity for vulnerable populations exposed to high TRAP.

Overall Conclusions

- Positive associations of asthma hospital encounters with UCD-CIT modeled POA were consistent with associations for CALINE-4 modeled TRAP and primary ambient air pollutant gases (NO_2, NO_x and CO) .

- Important POA sources included both on-road and off-road diesel and gas sources, as well as other anthropogenic sources and wood smoke.

- Associations with meat cooking could be due to high correlations with other pollutants.

Overall Conclusions

- Multipollutant models reveal relatively independent associations of asthma hospital encounters with $PM_{2.5}$ and O_3.

- O_3 was also not confounded by UCD/CIT SOA and POA or by CALINE4 TRAP.

- Since $PM_{2.5}$ is an uncharacterized metric, we observed confounding by variables representing primary pollutants in the cool season.

- SOA was not associated with asthma morbidity nor did it confound positive association with $PM_{2.5}$ in the warm season, possibly due to imprecision in SOA estimation.

Limitations

- No information on causal air pollutant constituents represented by TRAP variables, which represent many chemical components from common sources;

- Exposure error due to time subjects spent at non-residential locations plus indoor sources;

- CALINE4 models have inputs low temporal resolution;

- High correlations among POA sources partly due to common meteorological determinants;

- Only one station available for $PM_{2.5}$ versus four for gases;

- The only individual-level socioeconomic data available was health insurance status.

Future Needs

- New information on differences in association of asthma morbidity by multiple local and regional air pollutants and by particle source:

  - POA exposures from important sources (e.g., residential vehicular traffic and wintertime wood smoke),

  - Importance of ultrafine vs. larger particles,

  - Exposure to local TRAP vs. ambient air pollutants representing more homogenous background exposures ($PM_{2.5}$, criteria pollutant gases),

  - Multipollutant models suggest unmeasured PM components (SOA?), especially for warm season $PM_{2.5}$.

- Future research is needed to address uncertainty in modeled and ambient air pollutant variables that are likely acting as surrogates for causal chemical components.

- Interventions for minority children living in low income communities who are more vulnerable to the adverse effects of air pollution.

Coinvestigators:

Michael J. Kleeman   Department of Civil and Environmental Engineering, University of California, Davis

Wu Jun   Program in Public Health and Department of Epidemiology, School of Medicine, University of California, Irvine.

Dan Gillen   Department of Statistics, School of Information and Computer Sciences, University of California, Irvine

Bruce Nickerson   Division of Pulmonary Medicine, Children's Hospital of Orange County, Orange CA

Staff:

Thomas Tjoa   Department of Epidemiology

Graduate Students:

Sevan Gullesserian   Department of Statistics, UCI

Jianlin Hu   Dept. Civil and Environmental Engineering, UCD

Questions?